Posttraumatic stress following pregnancy and childbirth
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PART II

SPECIFIC POPULATIONS
POSTTRAUMATIC STRESS DISORDER, ANXIETY AND DEPRESSION FOLLOWING PREGNANCIES CONCEIVED THROUGH FERTILITY TREATMENTS

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ABSTRACT

Objectives
To compare the postpartum prevalence of Posttraumatic Stress Disorder (PTSD), anxiety and depression in women who conceived via medically assisted conception (MAC) and women who conceived naturally.

Methods
All women (n=907) who delivered under supervision of four independent midwifery practices and three hospitals in the Netherlands during a 3 month period were asked to complete questionnaires on demographic, logistic, psychosocial and obstetric characteristics two to six months postpartum. In this cross-sectional study PTSD was measured with the Traumatic Event Scale-B; anxiety and depression were measured with the Hospital Anxiety and Depression Scale.

Results
The response rate was 47% (428 participants). No significant differences were found in the prevalence of PTSD (0.0% vs. 1.3%; odds ratio [OR]= 0.0 (95% confidence interval [CI]: 0 - ∞)), anxiety (28.1% vs. 22.2%; OR=1.4 (CI: 0.6-3.1)) and depression (9.4% vs. 14.6% (OR= 0.6 (CI: 0.8-2.0)) between the 32 women who conceived via MAC and the 396 women who conceived naturally.

Conclusions
We did not find significant differences in the prevalence of PTSD, anxiety and depression between women who conceived via MAC and women who conceived naturally.

Keywords: anxiety, depression, IVF, MAC, postpartum, posttraumatic stress disorder
INTRODUCTION

In 2008, 3.2% of the 177,713 infants born in The Netherlands\(^1\) were born as a result of Medically Assisted Conceptions (MACs), such as Intrauterine Insemination (IUI), Ovulation Induction (OI), In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI). As in many Western societies\(^2\), the number of women treated with and babies born after these fertility treatments in the Netherlands is increasing. In thirteen years time, the percentage of infants born after IVF or ICSI\(^3\) in the Netherlands has doubled, from 1.3% in 1996 to 2.6% in 2009.\(^4,\)\(^5\)

Conceiving and giving birth to a desired child is assumed to be a happy life-event, particularly for a woman who has a history of infertility and has expended much effort in becoming a mother. However, the potential burden of infertility and infertility treatment can make the transition from infertility to pregnancy and to motherhood complex and emotional time.\(^6,\)\(^7\) It is known that infertility affects emotional well-being, satisfaction with life and self-esteem and that failed fertility treatment is associated with diminished life satisfaction, reduced self-confidence and substantial psychological distress.\(^6\) Several studies have reported high levels of distress, anxiety and depressive symptoms in women undergoing fertility treatment.\(^8\)\(^-\)\(^10\) Women who became pregnant as a result of IVF were more anxious during early pregnancy than those who conceived naturally.\(^11,\)\(^12\) These differences were no longer reported in late pregnancy and early parenthood and the effects of a latent infertility crisis were not prominent when the children were 1 year old, suggesting that distress disappears when IVF-treatment results in continuing pregnancy.\(^13\)\(^-\)\(^15\) However, formerly infertile women may fear being judged for ‘complaining after they finally got what they wanted’ (i.e., a continuing pregnancy), possibly resulting in an underestimation of the prevalence of psychological problems in these women.\(^16\) Following stress-coping models on adjustment to chronic stressors,\(^17\) our study focuses on the following mental conditions: posttraumatic stress disorder (PTSD), anxiety and depression.

PTSD is an anxiety disorder that can occur following the experience or witnessing of a traumatic life-threatening event. The prevalence of PTSD following childbirth in the Netherlands is 1.2%,\(^16\) which is in line with the 1-2% reported in other developed countries.\(^19\) To date, no studies have focused specifically on symptoms of PTSD in formerly infertile women during or after pregnancy.

Anxiety rates are generally higher in postpartum women than in the general population\(^20\) and one in eight women develops postpartum depression.\(^21\) Apart from the negative effects on the psychological well-being of the mother, anxiety and depression may also result in an impaired mother-infant relationship\(^22\) which can lead to negative effects on children’s emotional and behavioral development.\(^23\) Currently, little is known about the effects of MAC on postpartum well-being. A large systematic review\(^24\) presented an overview on how women adjust emotionally after IVF. Only 27 of the 706 studies had investigated the women’s emotional adjustment with standardized measures in relation to norm or control groups. None of these studies had explored
the postpartum prevalence of PTSD, anxiety or depression in women having conceived via IVF. Another systematic review\(^6\) revealed no differences in postpartum anxiety or depression between women who had conceived through IVF or ICSI and women who had conceived naturally. Recently, higher anxiety levels\(^{13}\) and more depressive symptoms\(^{24}\) have been demonstrated among the 25 women who conceived through fertility treatment at three months postpartum compared to 39 women who conceived naturally.

The aim of the current study is to investigate whether the prevalence rates of postpartum PTSD, anxiety and depression in women conceiving through MAC are higher than in women having conceived naturally.

**MATERIALS AND METHODS**

**Design and study population**

This study is part of a larger cross-sectional multi-center study on the prevalence of and risk factors for posttraumatic stress following childbirth in the Netherlands by Stramrood et al.\(^{18}\) The Netherlands has a rather unique echelon system in perinatal care. In primary care, pregnancy and delivery are monitored by a midwife or general practitioner and women can choose to deliver at home (23%), or in a homelike setting in a hospital or birth centre (11%)\(^{26}\) In case of (an increased risk for) complications or interventions during pregnancy or delivery, as defined by national guidelines\(^{26}\), women are referred to a gynecologist. The majority of women (66%) deliver under supervision of a gynecologist in a hospital (secondary care), or in an academic referral centre (tertiary care).\(^1\) This study was conducted in two general hospitals (Apeldoorn, Breda), one academic referral center (Groningen) and four midwifery practices in these same cities between November 2007 and January 2008. All women who gave birth between July and October 2007 at 16 weeks gestation or longer (including those who had a pregnancy termination or stillbirth) were invited to participate in the study. The study was approved by the Medical Ethics Committees of the three participating hospitals.

**Measures**

All 907 women who gave birth in the participating centers during the aforementioned time period, were invited to complete a 30-45 minute web based questionnaire, with questions on demographic factors, obstetric background, fertility history, logistic features of delivery and their mental well-being. Information about complications during pregnancy and delivery was obtained from medical histories. The following pregnancy complications were recorded: hypertension, preeclampsia / HELLP-syndrome (hemolysis, elevated liver enzymes, low platelets), antenatal blood loss, intrapartum death, congenital defects, preterm premature rupture of membranes and membranes ruptured longer than 24 hours. We considered the following as delivery complications: preterm delivery (<37 weeks), post term delivery (> 42 weeks), induction of labor, instrumental delivery, cesarean section, episiotomy, laceration, suturing in operating room, manual placenta removal,
postpartum hemorrhage (>1 liter), infection treated with antibiotics, patient admitted to Intensive Care Unit (ICU), meconium-stained amniotic fluid, asphyxia, infant admitted to N(I)CU, perinatal death and congenital malformations.

The Traumatic Event Scale-B (TES-B)\textsuperscript{27} and The Hospital Anxiety and Depression Scale (HADS)\textsuperscript{28} were used to screen for PTSD, anxiety and depression. The TES-B has been developed especially for measuring PTSD following childbirth. The internal consistency of the TES-B is good (Cronbach’s α coefficient was 0.87)\textsuperscript{29} Corresponding to the DSM-IV, at least 1 of 5 re-experiencing symptoms (criterion B), 3 of 7 avoidance symptoms (criterion C) and 2 of 5 hyperarousal symptoms (criterion D) should be present for the diagnosis PTSD to be considered. The 17 symptoms are rated on a four-point Likert-scale (0 to 3), where a minimum score of 2 (“sometimes”) is indicating a symptom to be present. The A criterion (traumatic experience) is met when women report to have felt fear, helplessness, or disgust during childbirth and when they also consider the childbirth as a trying experience or a threat to the physical integrity or life of themselves and/or the baby. The duration of symptoms (E criterion) should be at least one month, and women should rate the severity of the symptoms (criterion F) higher than 5 on a 10-point scale. To diagnose PTSD (dichotomized yes/no), all ABCDEF criteria have to be met. A sum score was calculated by adding the scores on the 17 symptom items.

The HADS\textsuperscript{28} is a frequently applied self-rating instrument for anxiety and depression. It has been designed especially for the hospital (somatic patient) setting, disregarding possible somatic components of depression and anxiety, in order to avoid confounding with symptoms of somatic conditions. The HADS was found to perform well in assessing the symptom severity of anxiety disorders and depression in somatic and psychiatric patients, as well as in primary care patients and in the general population.\textsuperscript{30} Furthermore, it has equally good sensitivity and specificity as other commonly used self-rating screening instruments.\textsuperscript{31} The HADS contains seven items for measuring anxiety and seven for depression, which are rated on a four-point-Likert scale from 0 to 3. To achieve optimal sensitivity and specificity (approximately 0.80), anxiety and depression were categorized into dichotomous variables, with a cut-off point of 8 or more on both scales\textsuperscript{30} for clinically significant anxiety and depression. A sum score can be calculated for anxiety by adding the score on the seven items for measuring anxiety. Similarly, adding the seven items for depression yields a depression sum score. The total HADS sum score can be computed by adding the scores on the fourteen items on anxiety and depression.

**Statistical Analysis**

Analyses were carried out using the Statistical Package for the Social Sciences (SPSS), version 16. The demographic and obstetric history of women who had conceived through MAC (MAC group) and women who had conceived naturally (NC group) was compared by using Mann-Whitney U-tests for the continuous, not normally distributed, dependent variables and \( \chi^2 \)-tests and Fisher’s exact tests for the categorical variables. Odds Ratios (ORs) were used to compare the prevalence of
PTSD, anxiety and depression in the MAC group to the NC group. Additionally, the effect of possible confounders was evaluated. A factor should be considered as a possible confounder if (a) it is associated with the exposing variable (MAC), (b) it is associated with one of more of the outcome variables (PTSD, anxiety, depression) and (c) the factor is known not to be part of the causal chain between exposing and outcome variables. Education, age, marital status, country of origin and the number of previous pregnancies were evaluated for a possible confounding effect on the comparison between the MAC and the NC-group. None of the variables were associated with both outcome and exposure at the p<0.10 level, and therefore no adjustment of the ORs was needed.

RESULTS

Of the 907 women invited to participate in the study, 428 completed the questionnaires (47%). Since information of the nonresponders is lacking, we compared data from the 428 participants to data from the entire Dutch population of childbearing women using nonparametric binomial tests. The percentages of home-births (20.1%) and deliveries in primary care setting (34.4%) in this study were comparable to that of the general population in the Netherlands (21.5% and 32.9%). Highly educated women and women >35 years were overrepresented in the sample, whereas non-western immigrants and women <25 years were underrepresented compared to the national average. There were more primiparous women (49.8%) than the national average (45.1%) and also more women with hypertension during pregnancy (11.4% vs. 7.6%). The proportion of women who conceived through fertility treatment in this sample was higher (7.5%) than to be expected from national data (3.2%).

From the 428 participants, 32 women had conceived through MAC (7.5%), and of those 15 women conceived via OI and IUI and 17 conceived via IVF/ICSI. The other 396 women had conceived naturally (NC group). The baseline characteristics of both groups are presented in table 1. No differences were found between the MAC group and NC group in education, marital status and country of origin, but the average age of the MAC group was significantly higher than the NC group (MAC: 33.7 years, NC: 31.7 years; p=.008). There were no differences in (a) the proportion of primiparous women, (b) the occurrence of terminations of pregnancy in history, (c) the proportion of women with complications during pregnancy or delivery and (d) the percentage of women delivering in a primary care setting. Of the recorded pregnancy and delivery complications, only the prevalence of hypertension was significantly different (MAC: 25.0%, NC: 10.4%; p=.012), especially in the IVF/ICSI group: 41.2% of these women had hypertension during pregnancy, compared to 10.2% of the women who conceived with other fertility treatment or naturally (OR= 6.2 (CI: 2.2-17.0)). In the MAC group more twins were born.
### Table 1. Population characteristics and differences between groups

<table>
<thead>
<tr>
<th></th>
<th>MAC (%)</th>
<th>NC (%)</th>
<th>Total (%)</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 32)</td>
<td>(n = 396)</td>
<td>(n = 428)</td>
<td></td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>Upper level Secondary / University</td>
<td>50.0%</td>
<td>55.3%</td>
<td>54.9%</td>
</tr>
<tr>
<td>Marital status</td>
<td>Living together / Married</td>
<td>100.0%</td>
<td>92.6%</td>
<td>96.5%</td>
</tr>
<tr>
<td>Country of origin</td>
<td>The Netherlands</td>
<td>96.6%</td>
<td>92.7%</td>
<td>93.0%</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td>Primiparity</td>
<td>62.5%</td>
<td>48.7%</td>
<td>49.8%</td>
</tr>
<tr>
<td>Miscarriage in history</td>
<td></td>
<td>25.0%</td>
<td>18.2%</td>
<td>18.7%</td>
</tr>
<tr>
<td>Terminations of pregnancy in history</td>
<td></td>
<td>0.0%</td>
<td>5.3%</td>
<td>4.9%</td>
</tr>
<tr>
<td>Ectopic pregnancy in history</td>
<td></td>
<td>3.1%</td>
<td>1.0%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Multiple pregnancy</td>
<td></td>
<td>9.4%</td>
<td>1.5%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Pregnancy complications</td>
<td></td>
<td>50.0%</td>
<td>46.0%</td>
<td>46.3%</td>
</tr>
<tr>
<td><strong>Delivery – logistics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Care setting</td>
<td>Primary</td>
<td>31.2%</td>
<td>34.7%</td>
<td>34.4%</td>
</tr>
<tr>
<td>Place of delivery</td>
<td>Home</td>
<td>15.6%</td>
<td>20.5%</td>
<td>20.1%</td>
</tr>
<tr>
<td></td>
<td>Hospital</td>
<td>71.9%</td>
<td>65.9%</td>
<td>66.4%</td>
</tr>
<tr>
<td></td>
<td>Referral from home to hospital</td>
<td>12.5%</td>
<td>13.6%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Supervision delivery</td>
<td>Midwife</td>
<td>40.6%</td>
<td>45.2%</td>
<td>44.9%</td>
</tr>
<tr>
<td></td>
<td>Gynecologist</td>
<td>37.5%</td>
<td>29.5%</td>
<td>30.1%</td>
</tr>
<tr>
<td></td>
<td>Midwife and gynecologist / other</td>
<td>21.9%</td>
<td>25.3%</td>
<td>24.0%</td>
</tr>
<tr>
<td>Delivery complications</td>
<td></td>
<td>35.5%</td>
<td>44.0%</td>
<td>43.4%</td>
</tr>
</tbody>
</table>

MAC= Medically Assisted Conception; NC=Natural conception; SD= standard deviation

* Chi-square or Fisher’s exact test: significant at p<.05 level

The prevalence of PTSD, the experience of a traumatic delivery, anxiety and depression in women after MAC compared to women who conceived naturally is summarized in table 2. The prevalence rates did not differ significantly between the groups. In addition, the mean TES-B sum score (MAC: 6.1, NC: 6.3; p=.866), the mean HADS anxiety sum score (MAC: 4.9, NC: 5.0; p=.851), the mean HADS depression sum score (MAC: 3.7, NC: 3.1; p=.405) and the mean total HADS sum score did not differ (MAC: 8.0, NC: 8.6; p=.458) between the two groups.
**Table 2. Prevalence of PTSD, traumatic childbirth, anxiety and depression in the MAC and NC groups**

<table>
<thead>
<tr>
<th></th>
<th>MAC (n = 32)</th>
<th>NC (n = 396)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD</td>
<td>0.0%</td>
<td>1.3%</td>
<td>0.0 (0 - ∞)</td>
</tr>
<tr>
<td>Traumatic childbirth</td>
<td>6.3%</td>
<td>9.3%</td>
<td>0.6 (0.2-2.8)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>28.1%</td>
<td>22.2%</td>
<td>1.4 (0.6-3.1)</td>
</tr>
<tr>
<td>Depression</td>
<td>9.4%</td>
<td>14.6%</td>
<td>0.6 (0.8-2.0)</td>
</tr>
</tbody>
</table>

MAC= Medically Assisted Conception; NC=Natural conception; OR=Odds Ratio of MAC compared to NC; CI=Confidence Interval

**DISCUSSION**

The aim of this study was to obtain insight into the postpartum well-being of women after MAC. To this end, data were collected on PTSD, anxiety and depression two to six months postpartum in women who conceived after MAC and a control sample. We found similar rates of postpartum mental well-being in women who became pregnant through MAC and women who conceived naturally. In terms of demographic variables the groups were comparable, with one exception: the mean age of the MAC-group was higher, which is well known from previous research, because of several years of attempting to conceive before commencing fertility treatment. On the other hand, the occurrence of miscarriages, pregnancy terminations and ectopic pregnancies did not differ between the groups, nor did the proportion of women delivering in a primary care setting under supervision of a midwife.

The comparable baseline characteristics of the MAC-group and NC-group enabled us to focus primarily on potential differences in prevalence of PTSD, anxiety and depression between the groups. As opposed to Monti et al., we did not find significant differences between them MAC and NC groups in the prevalence of PTSD, anxiety and depression. Monti’s case control, longitudinal study used other tests (ASQ-IPAT Anxiety Scale; Edinburgh Postnatal Depression Scale) to screen for anxiety and depression. In contrast with the HADS, the ASQ-IPAT anxiety scale is rarely used in pregnant or postpartum women. Furthermore, the study of Monti et al. did not take PTSD in account, was carried out in a hospital setting, only included in patients who conceived through undefined Assisted Reproductive Technologies (ART), had a smaller sample size (ART: n=25; controls: n=39) and had a lower response rate (30%) than our study. Although the study of Monti et al. found more symptoms of anxiety and depression after fertility treatment than natural conception, the prevalence of anxiety and depression in the clinical range was not higher. Monti et al. not only fail to specify which techniques are included in their definition of ART, but also do not mention on which guidelines their inclusion criteria are based. Therefore comparison with the current study should be done with caution.
Contrary to other studies\textsuperscript{33-35} no differences between the MAC and NC group were found in the incidence and nature of complications during pregnancy and delivery except for hypertension in pregnancy. A prolonged time to achieve pregnancy due to underlying sub fertility (and not the use of MAC) is a known risk factor for obstetrical and perinatal complications.\textsuperscript{33} Considering that ‘time to achieve pregnancy’ was not part of our questionnaire, a possible explanation is that our NC group also included formerly infertile women (i.e. those trying unsuccessfully to conceive for over a year) who did eventually become pregnant without fertility treatment. These women have been reported to suffer more from mental problems\textsuperscript{10} than women without reduced fertility. This may (partly) explain why no difference in complications was found between the MAC- and NC-group.

**Definition of MAC and ARTs**

A general point of concern is that in literature fertility treatments are sometimes referred to as MAC and sometimes as ARTs. Since definitions vary, comparison between studies should be done with caution. Some studies included in their definition of ART all acts that (a) separate sexual intercourse and reproduction and (b) include at least one other party, including donor insemination with or without medical assistance.\textsuperscript{36} Other studies distinguish between less invasive ART (such as IUI) and more invasive ART (such as IVF and ICSI)\textsuperscript{10} or use the term without specification.\textsuperscript{23,24} Fertility societies\textsuperscript{3} only refer to ART when both eggs and sperm are handled, i.e. only for IVF and ICSI. MAC refers to a broader range of fertility treatments\textsuperscript{9}, and all fertility treatments used in this study (IVF, ICSI, OI, IUI) may be referred to as MAC.

**Strengths**

One of the strengths of our study is the unselected population, which enables generalization to childbearing women in the Netherlands. Additionally, considering the absence of financial remuneration and the substantial time-investment required, we consider the response rate (47%) acceptable. The proportion of deliveries in primary care and home births in this study resemble the general population. The present study made use of outcome measures defined in terms of PTSD, anxiety and depression with proven reliability and validity and compared with norm groups. This study makes a distinction between symptoms of anxiety and depression, and meeting diagnostic criteria for a mental disorder. While some anxiety and depressive symptoms are common after childbirth (perhaps almost universal as most new mothers worry about the wellbeing of their baby and feel somewhat overwhelmed and unprepared for the challenges of caring for a newborn), major depressive disorder, PTSD and anxiety disorders, meeting diagnostic criteria are less common.

**Limitations**

There are limitations that must be considered in the interpretation of the results. In this study, more women conceived through fertility treatment (7.5%) than in the general population (3.2%), possibly because formerly infertile women are more willing to participate in these studies. Highly educated women were overrepresented in the sample, mainly in the first echelon, whereas nonwestern immigrants were underrepresented. Another limitation of the present study resides in
its retrospective design. We have taken special care to avoid sources of bias (unselected population) and we have evaluated the effect of possible confounders. Since we have used an existing database and we did not select the MAC group in advance, we dealt with a relatively small sample size. Post hoc power analysis showed that a difference in the prevalence of symptoms (PTSD, anxiety, depression) of 20% in our sample could have been detected with a power of 80%. Since the difference in prevalence rates proved <20%, a larger sample is recommended for future research, also because trends observed in the current study may prove to be significant differences when applying a larger sample size. The current results can be interpreted in two ways. On the one hand, the prevalence of PTSD, anxiety and depression in both groups did not differ significantly. Hence, there is no indication for extra or special psychological care postpartum for all women who gave birth following fertility treatment. On the other hand, the percentages of anxious (22.7%) and/or depressed (14.3%) women in both the MAC and the control groups are relevant in practice and should have clinical implications.

Studies show that the potential psychological burden of infertility and infertility treatment is cumulating the longer the infertility continues and the more the amount of (invasive) treatments increases. The lack of information about the time to achieve pregnancy and the number of fertility treatments women in the MAC group have undergone are limitations in this study. There is clear evidence that MAC results in more pregnancy and perinatal complications than natural conception. Other than hypertension, no difference in complications was found between the groups in this study, which is likely to be due to the relatively small number of women with MAC.

This is the first study to investigate the prevalence of PTSD following childbirth in women who conceived though MAC as compared to childbearing women without fertility problems and adds to the existing knowledge on the occurrence of anxiety and depression postpartum in formerly infertile women. Future studies should consider the time to achieve pregnancy, as research shows that increased risks for obstetrical and perinatal complications in formerly infertile women can be attributed to the underlying infertility and not to the use of fertility treatment. Another factor to consider is the emotional adjustment during the transition from infertility via pregnancy to motherhood and the role of support by family, friends and professionals in this process. Previously infertile women may tend to feel especially guilty complaining about pregnancy and motherhood when they have longed for it, thus, feeling a lack of entitlement to complain, now that have finally gotten what they have wanted for so long.

Often women who finally become pregnant after a period of infertility are considered to have “succeeded” in their fertility treatments and, as a result, are not paid as much attention from the medical community. On the other hand, sometimes there is unwarranted concern that new mothers after infertility may be more fragile than other mothers. In the Netherlands, the Obstetric Indication List (a screening system for identifying “physiological” and “pathological” pregnancies) considers the pregnancy and birth after subfertility as normal, with no indication
of an increased obstetric risk. Although it is important to consider the unique needs of this group of women, our study indicates that previously infertile new mothers experience mental well-being similar to their fertile counterparts with no more referral to the second or tertiary care setting.

In conclusion, in this study no significant differences were found in the prevalence of PTSD, anxiety and depression between women who conceived through fertility treatment and women who conceived naturally. Only the prevalence of hypertension was higher in the IVF/ICSI group. Since we dealt with a relatively small sample size, further research on a larger scale with additional attention to the time to achieve pregnancy and the needs, demands and consumption of prenatal and postnatal care of previously infertile women is desired.
REFERENCES


POSTTRAUMATIC STRESS DISORDER FOLLOWING PREECLAMPSIA AND PPROM:
A PROSPECTIVE STUDY WITH 15 MONTHS FOLLOW-UP

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ABSTRACT

Objectives
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.

Conclusions
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, while 1 in 8 are depressed during pregnancy or postpartum. These conditions affect not only the women involved but may also impair secure attachment of the infant and affect the partner relationship. 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 re-experiencing 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. Posttraumatic stress disorder commonly co-occurs with major depressive disorder.

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. Accordingly, one may hypothesize that the prevalence of PTSD is higher among women with complicated pregnancies. Complications are often associated with interventions and lengthy hospitalization of the infant. Pregnancy may be complicated by conditions that are potentially life threatening for the fetus (e.g., preterm premature rupture of membranes [PPROM]) or both mother and fetus (e.g., 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 at 28% in an exploratory retrospective study in Dutch patients with PE. 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.

Several studies suggest that vulnerability for psychological problems (i.e., 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. 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, while other researchers found little change over time.

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\(^7\) 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 (i.e., 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 (ISSHP).\(^18\) 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\(^6\), we assumed a moderate effect size (\(w = .30\)). Combined with an \(\alpha\) of .01 and a desired power (\(\beta\)) 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 (t₁), 6 weeks postpartum (t₂), and 15 months postpartum (t₃). In order to obtain comparable intervals between t₁ and t₃ in the patient and control groups, participants in the control group were tested in the 38th week of pregnancy.

Measures
At t₁, 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 (e.g., with nightmares or intrusive thoughts)?” Interviewers were blind to questionnaire results. At t₁ 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 .74.²⁸ In the present sample, the internal consistency was good (α = .86 at t₁, α = .94 at t₂, and α = .89 at t₃). The PSS-SR that was administered at t₁ asked for PTSD symptoms in the preceding month that were related to any stressful event experienced before that still bothered the participants. At t₂ and t₃, the PSS-SR referred to PTSD symptoms in the preceding month that were specifically related to pregnancy and the perinatal period. In addition, at t₃, 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. More specifically, pregnancy-related PTSD was considered present when participants (a) scored 80 or more on 1 of the VAS for horror, fear, and/or helplessness at \( t_2 \) (subjective stress, DSM-IV A2 criterion); (b) reported at least 1 re-experiencing, 3 avoidance, and 2 hyperarousal 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; (c) 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 \( t_2 \) the same criteria were used except for the VAS scores. Women with PTSD at \( t_2 \) but not at \( t_1 \) 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, \( \chi^2 \) analyses were used. Comparing participants to non-responders 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 non-parametrical 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, non-normally 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 non-responders 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 drop-out.](image)

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 non-responder analysis at
t₃ were used, with the addition of the proportion of women with PTSD and depression at t₃. Women with PE who did not participate at t₃ 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 t₃. 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 t₃. No significant differences were found between the 3 controls not participating at t₃, as compared to the 62 healthy controls completing all 3 measurements.

Demographic and obstetric characteristics of the 175 women participating at t₃ 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.

**Table 1. Demographic, psychiatric & obstetric characteristics of women participating at t₃ (n=175)**

<table>
<thead>
<tr>
<th></th>
<th>PE (n = 57)</th>
<th>PPROM (n = 53)</th>
<th>Control (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age y (SD)*</td>
<td>29.4 (5.1)</td>
<td>30.7 (4.8)</td>
<td>31.9 (3.9)</td>
</tr>
<tr>
<td>Married or co-habit ing n (%)</td>
<td>54 (100%)</td>
<td>47 (92%)</td>
<td>61 (95%)</td>
</tr>
<tr>
<td>Completed college or University n (%)*</td>
<td>19 (34%)</td>
<td>19 (36%)</td>
<td>54 (83%)</td>
</tr>
<tr>
<td>Not employed n (%)</td>
<td>5 (9%)</td>
<td>10 (19%)</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Psychiatric history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reported history of depression n (%)</td>
<td>22 (39%)</td>
<td>18 (34%)</td>
<td>17 (26%)</td>
</tr>
<tr>
<td>Reported history of PTSD n (%)</td>
<td>7 (13%)</td>
<td>13 (25%)</td>
<td>9 (14%)</td>
</tr>
<tr>
<td>Obstetric characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primipara **</td>
<td>43 (80%)</td>
<td>25 (49%)</td>
<td>48 (74%)</td>
</tr>
<tr>
<td>Hospitalization mother d (SD) *</td>
<td>9.4 (9.1)</td>
<td>18.6 (22.2)</td>
<td>0</td>
</tr>
<tr>
<td>Cesarean delivery n (%) *</td>
<td>43 (77%)</td>
<td>15 (28%)</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Gestational Age wk+dy (SD) *</td>
<td>31+3 (3.9)</td>
<td>31+3 (3.2)</td>
<td>40+5 (1.0)</td>
</tr>
<tr>
<td>Birth weight g (SD) *</td>
<td>1506 (846)</td>
<td>1686 (638)</td>
<td>3703 (500)</td>
</tr>
<tr>
<td>10-min APGAR score (SD) *</td>
<td>7.5 (2.1)</td>
<td>7.7 (2.2)</td>
<td>9.4 (1.0)</td>
</tr>
<tr>
<td>Death of infant n (%) *</td>
<td>7 (12.3%)</td>
<td>5 (9.4%)</td>
<td>0</td>
</tr>
<tr>
<td>Infant hospitalized at t₃ n (%)*</td>
<td>24 (43%)</td>
<td>20 (39%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Demographic characteristics and psychiatric history collected at t₃,
Obstetric characteristics collected at t₃
* Significant difference between control group and patient groups
** Significant difference between PPROM and all other groups
Prevalence
At t₂, 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 t₂ and t₃. Pearson χ² tests indicated significant differences between the 3 groups in the prevalence of PTSD at both time points (t₂: p=.039; t₃: p=.018): the prevalence of PTSD was significantly higher in the patient group (PE and PPROM combined) than in the control group (t₂: χ²= 5.194, p=.023; t₃: Fisher exact test p=.032). There were no significant differences in the prevalence of PTSD between the PE and the PPROM group (t₂: χ²= 0.972, p=.324; t₃: Fisher exact test p=.391). Figure 3 shows the prevalence of depression at t₄, t₅, and t₆. The 3 groups did not differ significantly with respect to the prevalence of depression at either of the 3 time points.

At t₅, 9 (53%) of the 17 women with PTSD also had a co-morbid depression. Further exploration of the data using non-parametric Mann-Whitney U tests revealed that at t₅, symptoms of PTSD and depression were associated with depression in history, depression at t₄, and PTSD at t₁ but not to a history of PTSD (all independent variables dichotomized). Women with PTSD and depression in history, during pregnancy (t₁) and at 6 weeks postpartum (t₄) reported more symptoms of PTSD and depression at t₅.

Of the 17 women with PTSD at t₅, 8 did not participate at t₆. Of the 9 women who did participate at t₅, 2 still met the criteria for PTSD at 15 months follow-up. In all, 7 women no longer met the PTSD criteria at t₅, 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 t₅; that is, women who did not meet the criteria for PTSD at t₅.

Risk Factors
As the death of an infant in the postpartum period is extremely stressful and can induce “grief-associated depressive symptoms”⁹⁴, we investigated the effect of the death of the infant on the prevalence of depression and PTSD at t₅. The results, summarized in table 2, indicate that the prevalence of depression and PTSD, as well as the sum scores on the PSS-SR and BDI were significantly higher in women who had lost their infants (all p’s<.01). In order to evaluate whether removing the 12 women whose infants had died would influence the differences in prevalence rates, we repeated the χ² tests for PTSD at t₅ for n=163. Prevalence rates decreased from 10.5% to 6.0% in 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 t₅ did not persist (p=.062). However, the difference between women with PPROM and controls was significant (Fisher exact test 2-tailed: p=.035).
Figure 2. Prevalence of PTSD related to pregnancy and childbirth at t2 and t3

Figure 3. Prevalence of depression at t2, t2 and t3
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 \( t_1 \)).

<table>
<thead>
<tr>
<th></th>
<th>Living infant (n = 98)</th>
<th>Infant died (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD *</td>
<td>10 (10%)</td>
<td>5 (42%)</td>
</tr>
<tr>
<td>Depression*</td>
<td>7 (7%)</td>
<td>5 (42%)</td>
</tr>
<tr>
<td>PSS-SR score *</td>
<td>10.0 (6.0-17.2)</td>
<td>24.4 (18.2-37.5)</td>
</tr>
<tr>
<td>BDI score*</td>
<td>8.5 (5.0-12.4)</td>
<td>16.1 (9.8-30.2)</td>
</tr>
</tbody>
</table>

* Significant difference between women with a living infant and women whose infant died between \( t_1 \) and \( t_2 \).

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 (\( \chi^2 \) 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 \( t_2 \), 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 \( t_j \)) 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).\(^9\) 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 \( t_j \) 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 \( t_1 \)) 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\(^6\) 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 \( t_1 \) 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.\(^6\)

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 (i.e., 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 (i.e., \( n = 1388 \)).\(^20\) 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 (i.e., 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. 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, 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 (e.g., 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 and illustrate the major impact of losing a child 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 (e.g., 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 (e.g., BDI-II or Edinburgh Postnatal Depression Scale), 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: 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.\textsuperscript{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.
REFERENCES


FATHERS WITH PTSD AND DEPRESSION IN PREGNANCIES COMPLICATED BY PRETERM PREECLAMPSIA OR PPROM

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ABSTRACT

Objectives
To assess prevalence and risk factors for posttraumatic stress disorder (PTSD) and depression in fathers after early preeclampsia (PE) or preterm premature rupture of membranes (PPROM).

Methods
Partners of patients hospitalized for PE or PPROM and partners of healthy controls completed PTSD (PSS-SR) and depression (BDI-II) questionnaires during pregnancy (t₁) and six weeks postpartum (t₂). 85 of the 187 eligible men participated (51 partners of patients, 34 partners of controls) at t₁ and 66 men participated both time points.

Results
No significant differences were found between partners of patients and partners of controls in symptoms of PTSD and depression (t₁: p=.28 for PTSD and p=.34 for depression; t₂: p=.08 for PTSD and p=.31 for depression). For partners of patients, correlation between PTSD and depression sum-scores was .48 (p<.001) at t₁ and .86 (p<.001) at t₂. Within-couple correlation was low and not significant during pregnancy, but strong postpartum (PSS-SR: r=.62, p<.001; BDI-II: r=.59, p<.001). Higher paternal age was associated with more symptoms of PTSD and depression postpartum in partners of patients. Symptoms of PTSD and depression during pregnancy predicted the occurrence of PTSD symptoms following childbirth in partners of patients.

Conclusions
Symptoms of PTSD and depression occurred at a similar rate in partners of women with PE or PPROM and partners of healthy pregnant controls. Symptoms of PTSD and depression during pregnancy predicted the occurrence of PTSD symptoms following childbirth. Increased paternal age predicted more symptoms of PTSD and depression postpartum. At six weeks postpartum, a strong association was found between men and women in symptoms of PTSD and depression.

Keywords: PTSD; depression; fathers; postpartum; preeclampsia; PPROM
INTRODUCTION

Depression affects roughly 12% of women during pregnancy and 7% postpartum\(^1\), whereas posttraumatic stress disorder (PTSD) following childbirth and pregnancy occurs after 1 to 2% of deliveries.\(^2,3\) Next to affecting the well being of the woman, both postpartum depression (PPD) and PTSD may impair secure attachment of the infant and affect the partner relationship.\(^4,5\) Contrary to a commonly held belief, the birth of a child can trigger the onset of mental problems and psychiatric illnesses in fathers as well\(^6\), and their mental well being is known to affect the parent-child relationship, and child behavioral and emotional development.\(^7,9\)

Whether or not prevalence rates of depression are similar in men and women is under debate, as various studies find contradictory results.\(^10-14\) A substantial amount of research has been carried out regarding postpartum depression in men, and a recent meta-analysis estimated the prevalence at 10.4%.\(^15\) The strongest predictor for paternal depression is maternal postpartum depression, as it affects 24-50% of the partners of women with postpartum depression.\(^16\)

A limited number of recent studies have investigated the occurrence of PTSD following childbirth in men. PTSD is an anxiety disorder that may develop following confrontation with a traumatic stressor, with three categories of characteristic symptoms: re-experiencing of the event, avoidance of stimuli associated with the event, and hyperarousal.\(^17\) The DSM-IV states that in order to qualify for PTSD, a traumatic event may also be witnessed (as partners do) rather than experienced (by the pregnant woman), but the actual experience of “threat to own life” is considered a strong predictor for the development of PTSD.\(^18\) In a retrospective study by Bradley et al.\(^19\), 199 fathers of healthy newborns who were present during the hospital birth were assessed six weeks following childbirth. No men were found to have PTSD, although 12% reported symptoms on at least one of the three PTSD symptom categories. Clinically significant symptoms of depression and anxiety were found in 8 and 7% of fathers, respectively. Skari et al\(^20\) included both mothers and fathers, and found significant levels of acute distress and intrusive symptoms (DSM-IV criterion C as measured with the Impact of Events Scale (IES)\(^20\) during the first four days after delivery. Symptoms were more frequent in women than in men, but no full constellation of PTSD symptoms was found in any subject. In a study by Ayers et al.\(^21\) 5% of women and men scored above the recommended cut-off for both avoidance and intrusion on the IES. Even though the similar rates in men and women are not in line with other literature, it is of interest that the six cases were two couples and two individuals, suggesting a concordance between couples, as is known from studies on postpartum depression. A recent study by Iles et al.\(^14\) found that symptoms of PTSD were significantly related within couples, and that dissatisfaction with partner support and less secure attachment were associated with higher levels of posttraumatic stress and depression postpartum.

In women, several studies showed significantly higher PTSD rates after preterm delivery (due to various causes) compared to uncomplicated pregnancies.\(^22-30\) Only one prior study has thus far
looked at PTSD in partners of women with severe pregnancy complications. Pierrehumbert et al. assessed PTSD in parents of infants born prematurely (25-33 weeks gestation). Both mothers and fathers were found to have more posttraumatic stress (symptoms) than parents of healthy infants born at term. In this retrospective study, parents were assessed 18 months after delivery. This is long, considering that the chance of other causes for PTSD increases with time, subsequent pregnancies and deliveries may have occurred in the mean time, and the longitudinal course of PTSD following childbirth is not sufficiently clear. Furthermore, the perinatal PTSD questionnaire (PPQ) used in Pierrehumbert’s study does not contain all DSM-IV criteria for PTSD, which has been noted as a point of concern. In a study involving the current sample that we published recently, 14% of women hospitalized for preeclampsia (PE) or preterm premature rupture of membranes (PPROM) fulfilled the DSM-IV criteria for PTSD on the PTSD Symptom Scale self report questionnaire (PSS-SR) at six weeks postpartum, and 11% were at least moderately depressed based on the Beck Depression Inventory, second edition (BDI-II). These data, as well as the identified risk factors for women (history of depression, depressive symptoms during pregnancy, perinatal mortality), made us inquire into the mental wellbeing of partners of women with pregnancy complications.

The present study included three main research questions with corresponding hypotheses: (1) What is the occurrence of symptoms of PTSD and depression during pregnancy and postpartum, in partners of women with complicated pregnancies, as compared to partners of women with uneventful pregnancies. Based on the findings of our study of women with PE/PPROM and healthy pregnant controls, we hypothesized that partners of patients would report more symptoms of PTSD and depression than partners of controls; (2) Is there a relation between symptoms of PTSD and depression in women and men? We hypothesized a moderate to strong correlation between partners, both during pregnancy and postpartum; (3) Which factors predict the occurrence of symptoms of PTSD and depression in partners of patients at six weeks postpartum? Based on previous studies conducted among women, we hypothesized that demographic factors would not be related to psychiatric symptoms, but obstetric factors and symptoms of PTSD and depression during pregnancy would predict the occurrence of symptoms in men postpartum.

METHODS

Design and setting
In this longitudinal study, pregnant women with PE or HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), and women with PPROM took part. PE was defined according to the American Congress of Obstetricians and Gynecologists’ (ACOG) practice bulletin on preeclampsia and eclampsia: a systolic blood pressure of 140 mm Hg or more, or a diastolic blood pressure of 90 mm Hg or more, in a previously normotensive woman after 20 weeks gestation, combined with the presence of 0.3 g or more of protein in a 24-hour urine specimen. HELLP syndrome was defined as aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) > 50 IU/L, and platelets < 100 * 10^9/L, and lactate dehydrogenase > 600 IU/L. Preterm premature rupture of membranes
(PPROM) was defined according to the ACOG practice bulletin on PROM\(^{36}\): rupture of membranes prior to the onset of labor and before 37 weeks of gestation. The female patients were recruited in the obstetric clinic of a University hospital in The Netherlands during a three year period. Healthy female controls with uneventful pregnancies were recruited in a community midwifery practice by means of posters announcing the study. Results of the mothers (patients and controls) have been published previously.\(^{30}\)

**Population**

All women hospitalized for PE and 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 treatment, or (c) they were too ill to complete questionnaires. Additional exclusion criteria were current multiple pregnancy, a history of intrauterine fetal death, and current alcohol or drugs dependence (of the pregnant woman). 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. Partners of patients and partners of controls were invited to take part in the study, though women could also take part if their partner refused. No further exclusion criteria were applied for the partners. Participants had to be fluent in Dutch and give written informed consent. Approval was obtained from the Medical Ethics Committee (Institutional Review Board) of the University Medical Center.

**Procedure**

Upon admission, patients and their partners were informed about the study and were asked to consider their participation within 24 hours. Female controls and their partners could sign up for the study through their community midwife. Following signed informed consent, they were contacted by one of the researchers and asked to complete questionnaires as soon as possible in order to minimize the loss of participants due to delivery before testing. Participants were tested during pregnancy (t\(_1\)) and six weeks postpartum (t\(_2\)). In order to obtain comparable intervals between t\(_1\) and t\(_2\) in the patient- and control groups, female controls and their partners were tested in the 38\(^{th}\) week of pregnancy.

**Measures**

At t\(_1\), all participants (male and female) completed a brief self-report measure of general demographic information, and answered questions about previous psychiatric history: (a) whether they had ever had “one or more periods of feeling depressed or down for most of the day, during which they were not interested in activities that they enjoyed before”, indicating depressive symptoms; (b) whether they had “ever experienced something traumatic” (including some examples) and “whether this influenced them afterwards, for example through nightmares or flashbacks”, indicating posttraumatic stress symptoms. Data regarding current and past obstetric status were collected from the medical record of the female patients and controls.
During both test-sessions, the PTSD Symptom Scale self report questionnaire (PSS-SR)\textsuperscript{12} and the Beck Depression Inventory, second edition (BDI-II)\textsuperscript{31}, were completed. The PSS-SR is a frequently used self report measure of PTSD symptoms. The questionnaire contains 17 items corresponding to the 17 PTSD symptoms described in the DSM-IV (criteria B, C and D). These items are rated using 4-point scales asking for the occurrence of each symptom over the past month (0 = never/not at all, 1 = once a week/a little bit, 2 = two to four times a week/somewhat, 3 = more than five times a week/very much). Symptoms were considered present if an item was rated 2 or 3. The PSS-SR sum-score ranges from 0 to 51. 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 $t_2$, 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 (3.9 inch) Visual Analogue Scales (VAS). Using visual analogue scales is a reliable method to assess pain, anxiety and mood disorders that is frequently used in both research and hospital settings.\textsuperscript{37-39} The 100 mm strip depicts a linear continuum from experiencing no pain or a certain emotion (0), to experiencing the worst imaginable pain or most intense emotion (100). Recent research concludes that VAS scales approximate an interval-scale level, and therefore have superior psychometric properties as compared to ordinal-scale categorical measures such as Likert scales.\textsuperscript{40} In the present study, PTSD diagnosis at $t_2$ was based on a symptom profile reflected by the PSS-SR and VAS scores that were consistent with the DSM-IV criteria. For this, we used the criteria as used in the study by Engelhard et al.\textsuperscript{22} More specifically, pregnancy-related PTSD was considered present when participants (a) scored 80 or more on one of the VAS for horror, fear, and/or helplessness at $t_2$ (subjective stress, DSM-IV A2 criterion); (b) reported at least one re-experiencing, three avoidance, and two hyperarousal symptoms on the PSS (DSM-IV, B, C, and D criterion, respectively); (c) obtained a total PSS-SR score of 18 or higher (severity, DSM-IV F criterion). It should be noted that the duration criterion of four weeks (DSM-IV E criterion) was met because follow-up assessment was at six weeks and postpartum. The test-retest reliability has been calculated $\alpha=.74.32$ The PSS-SR has been validated in the Netherlands in a non-pregnant population, with $\alpha=.93$, sensitivity between .80 and .90, and specificity between .84 and .88.\textsuperscript{41} The BDI-II\textsuperscript{33} is a self-report measure of depressive symptoms during the preceding two weeks. It consists of 21 items containing four statements that reflect increasing symptom severity (scoring 0-3 per item). The sum-score ranges from 0 to 63. A cut-off score of 20 or more was used, corresponding with moderate depression according to the BDI manual.\textsuperscript{33} The BDI-II is one of the most frequently used depression instruments in clinical psychological settings, and found to have good psychometric properties in both clinical samples and the general population.\textsuperscript{33,42-44} The Dutch version has been validated in non-pregnant patient groups.\textsuperscript{45,46} As opposed to some other depression questionnaires, the BDI includes all DSM-IV symptom criteria, and allows for differentiation between somatic and non-somatic symptoms.
Statistical analysis
Data were analyzed with SPSS 16.0, using a significance level of .05 (two-tailed). For the dichotomous data, $X^2$ analyses were used. Exploration of the continuous data revealed that the PSS and BDI sum scores were not normally distributed. Therefore, non-parametrical Spearman's rho, Kruskal-Wallis and Mann-Whitney U-tests were used. In order to identify risk factors for PTSD and depression at $t_2$, stepwise multiple regression analyses (SMRA) were performed on the PSS and BDI sum scores. Where appropriate, non-normally distributed variables were square root transformed (SQRT) to meet assumptions of normality, linearity, and homoscedasticity. Due to the relatively small sample size (and therefore low number of variables desired in the SMRA), we only included variables with a p-value lower than .05 as found in univariate analyses in the SMRA. In order to evaluate the contribution of mental well being of female patients and their partners at $t_2$ to the PSS-SR and BDI scores, a stepwise model was created, entering factors known at $t_1$ in the first step, followed by factors known at $t_2$ in the second step. Two sets of variables showed multicollinearity: PSS-SR and BDI scores at $t_2$ in partners of patients, and PSS-SR and BDI scores at $t_1$ in female patients. Therefore, the PSS-SR scores of female patients and partners of patients at $t_2$ were excluded from the depression model and similarly, the BDI scores of female patients and partners of patients at $t_2$ were excluded from the PTSD model.

RESULTS
Patient characteristics
At $t_1$, 193 females (patients and controls) were included in the study, of whom six did not have a partner. Of the 187 eligible partners (all male), 85 agreed to participate at $t_1$ (45%). Non-responder analysis (using t-tests, chi square and Fisher’s exact tests) demonstrated that women whose partners did and did not participate were comparable for demographic factors (age, education, marital status), obstetric factors (primiparity, cesarean rate, gestational age at delivery, perinatal mortality) and symptoms of PTSD and depression in history, at $t_1$ and at $t_2$.

At $t_2$, 66 men completed questionnaires, whereas 19 men declined further participation (see figure 1). No significant differences were found between partners of controls participating at both $t_1$ and $t_2$ versus partners of controls only participating at $t_1$. Between partners of patients participating at both $t_1$ and $t_2$ versus those only participating at $t_1$, the only significant difference was that the 37 full participants reported fewer PTSD symptoms at $t_1$ than the 14 men who dropped out after $t_1$ (p=.021). In absolute numbers, the three partners of patients with PTSD during pregnancy and the two partners of patients with depression during pregnancy, did not participate at $t_1$. No differences were found in demographic, obstetric and psychological characteristics between men whose partner had PE and men whose partner was hospitalized with PPROM, except that primiparity and cesarean section were more common among women with PE than PPROM. Further analyses have therefore
been performed with the two groups combined. Demographic and obstetric characteristics of the 66 men participating at t₂, including differences between partners of patients and partners of controls, are shown in table 1.

**Figure 1. Overview of participation and drop out (n=)**

- **t₁** = during pregnancy
- **t₂** = 6 weeks postpartum

**Table 1. Characteristics of partners participating at t₂ (n= 66)**

<table>
<thead>
<tr>
<th></th>
<th>Partners of patients (n=37)</th>
<th>Partners of controls (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age <em>mean (SD)</em></td>
<td>31 (5.3)</td>
<td>34 (3.5)</td>
</tr>
<tr>
<td>Higher education % (N/total)</td>
<td>33 (12/36)</td>
<td>90 (26/29)</td>
</tr>
<tr>
<td>Employed % (N/total)</td>
<td>100 (35/35)</td>
<td>97 (28/29)</td>
</tr>
<tr>
<td><strong>Psychiatric history</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reported history of depression % (N/total)</td>
<td>25 (9/36)</td>
<td>35 (10/29)</td>
</tr>
<tr>
<td>Reported history of PTSD % (N/total)</td>
<td>14 (5/36)</td>
<td>24 (7/29)</td>
</tr>
<tr>
<td>Previous treatment for psychiatric problems % (N/total)</td>
<td>11 (4/37)</td>
<td>24 (7/29)</td>
</tr>
<tr>
<td>Current treatment for psychiatric problems % (N/total)</td>
<td>0 (0/37)</td>
<td>17 (5/29)</td>
</tr>
<tr>
<td><strong>Obstetric characteristics (females)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primipara % (N/total)</td>
<td>64 (23/36)</td>
<td>72 (21/29)</td>
</tr>
<tr>
<td>Cesarean section % (N/total)</td>
<td>59 (22/37)</td>
<td>3 (1/29)</td>
</tr>
<tr>
<td>Gestational age (weeks) <em>mean (SD)</em></td>
<td>31+6 (3+2)</td>
<td>40+5 (0+6)</td>
</tr>
<tr>
<td>Infant death % (N/total)</td>
<td>8 (3/37)</td>
<td>0 (0/29)</td>
</tr>
</tbody>
</table>

Demographics and psychiatric history collected at t₁, obstetric characteristics collected at t₂.

* p ≤ 0.05
Prevalence of symptoms of PTSD and depression
No significant differences were found between partners of patients and partners of controls in symptoms of PTSD and depression. At t₁, the mean sum-score on the 17 PSS-SR items was 6.9 for partners of patients and 4.6 for partners of controls (p=.28), and the mean sum-score on the 21 BDI-II items was 7.0 for partners of patients and 5.6 for partners of controls (p=.34); at t₂, the mean sum-score on the 17 PSS-SR items was 6.5 for partners of patients and 3.1 for partners of controls (p=.08), and the mean sum-score on the 21 BDI-II items was 5.6 for partners of patients and 3.9 for partners of controls (p=.31). In partners of patients, the correlation between PTSD and depression sum-scores was .48 (p<.001) during pregnancy, and .86 (p<.001) postpartum. For partners of controls, the correlation between PTSD and depression sum-scores was .60 (p<.001) during pregnancy, and .73 (p<.001) postpartum. No men met the DSM-IV criteria for both disorders simultaneously.

Relation between paternal and maternal symptoms
Within-couple correlation of PTSD and depression symptom severity was low and not significant during pregnancy (PSS-SR: r=.24, p=.159; BDI-II: r=.17, p=.303), but strong postpartum (PSS-SR: r=.62, p<.001; BDI-II: r=.59, p<.001).

Tables 2 and 3 display the associations between symptoms of PTSD/depression in partners of patients at t₂ and several demographic, obstetric and psychiatric factors. In partners of patients, PTSD and depressive symptoms postpartum (t₂) were associated with PTSD and depression at t₁, with concurrent PTSD and depression (at t₁) in their female partners, but not with a history of depression or PTSD in either female patients or their partners. Furthermore, lower gestational age at delivery, infant death and higher paternal age were associated with more symptoms of PTSD and depression at t₂, whereas parity and mode of delivery were unrelated to PTSD/depression postpartum in partners of patients.

Evaluation of possible risk factors
Finally, we evaluated the partners of patients for the contribution of risk factors to the PSS-SR and BDI scores at t₂ using two stepwise multiple regression analyses. All variables with a p-value of 0.05 or lower in the univariate analyses (table 3) were included.

Table 4 shows the SMRA for PTSD symptoms (PSS-SR sum scores) of partners of patients at t₂. The model for SQRT PSS-SR at t₂ explained 53% (adjusted R²) of the variance in the PSS-SR sum scores in the first step (Sig. F change <.001), while the second step was not significant (sig. F change = .074). Significant predictors of high paternal PSS-SR sum-scores at t₂ were PSS-SR and BDI sum-scores in men at t₁ and higher paternal age (table 4).
Table 2. Spearman’s Rho correlations between PTSD/depressive symptoms and demographic, obstetric and psychiatric characteristics for partners of patients participating at \( t_1 \) (n=37)

<table>
<thead>
<tr>
<th></th>
<th>PTSD symptoms (r=)</th>
<th>p=</th>
<th>Depressive symptoms (r=)</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic and obstetric variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.376</td>
<td>.026 *</td>
<td>.367</td>
<td>.030 *</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>-.471</td>
<td>.003 **</td>
<td>-.423</td>
<td>.009 **</td>
</tr>
<tr>
<td><strong>Psychiatric history (partners of patients)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSD symptoms ( t_1 )</td>
<td>.456</td>
<td>.005 **</td>
<td>.411</td>
<td>.012 *</td>
</tr>
<tr>
<td>Depressive symptoms ( t_1 )</td>
<td>.558</td>
<td>&lt;.001 ***</td>
<td>.671</td>
<td>&lt;.001 ***</td>
</tr>
<tr>
<td>PTSD symptoms ( t_2 )</td>
<td></td>
<td></td>
<td>.858</td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms ( t_2 )</td>
<td>.858</td>
<td>&lt;.001 ***</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td><strong>Psychiatric history (female patients)</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSD symptoms ( t_1 )</td>
<td>.357</td>
<td>.030 *</td>
<td>.179</td>
<td>.289</td>
</tr>
<tr>
<td>Depressive symptoms ( t_1 )</td>
<td>.149</td>
<td>.378</td>
<td>.075</td>
<td>.657</td>
</tr>
<tr>
<td>PTSD symptoms ( t_2 )</td>
<td>.624</td>
<td>&lt;.001 ***</td>
<td>.531</td>
<td>&lt;.001 ***</td>
</tr>
<tr>
<td>Depressive symptoms ( t_2 )</td>
<td>.625</td>
<td>&lt;.001 ***</td>
<td>.586</td>
<td>&lt;.001 ***</td>
</tr>
</tbody>
</table>

* p<.05; ** p<.01; *** p<.001

Table 3. Associations between PTSD/depressive symptoms and demographic, obstetric and psychiatric characteristics for partners of patients participating at \( t_2 \) (n=37)

<table>
<thead>
<tr>
<th></th>
<th>PTSD symptoms p=</th>
<th>Depressive symptoms p=</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic and obstetric variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher/lower education (partners)</td>
<td>.245</td>
<td>.045 *</td>
</tr>
<tr>
<td>Primipara</td>
<td>.585</td>
<td>.791</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>.926</td>
<td>.652</td>
</tr>
<tr>
<td>Infant death</td>
<td>.016 *</td>
<td>.011 *</td>
</tr>
<tr>
<td><strong>Psychiatric history (partners of patients)</strong></td>
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<td></td>
</tr>
<tr>
<td>PTSD symptoms in history</td>
<td>.232</td>
<td>.089</td>
</tr>
<tr>
<td>Depressive symptoms in history</td>
<td>.226</td>
<td>.199</td>
</tr>
<tr>
<td><strong>Psychiatric history (female patients)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSD symptoms in history</td>
<td>.494</td>
<td>.888</td>
</tr>
<tr>
<td>Depressive symptoms in history</td>
<td>.133</td>
<td>.515</td>
</tr>
</tbody>
</table>

* p<.05

Mann Whitney U-tests: comparison between those with and without the characteristic
Table 4. Stepwise Hierarchical Multiple Regression Analysis of PTSD symptoms in partners of patients at t₁ (n=37)

<table>
<thead>
<tr>
<th></th>
<th>Adj. R²</th>
<th>Δ R²</th>
<th>Beta</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1: Factors known at t₁</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms at t₁ (partners)</td>
<td>.533</td>
<td>.553</td>
<td>.338</td>
<td>*</td>
</tr>
<tr>
<td>PTSD symptoms at t₁ (partners)</td>
<td></td>
<td></td>
<td>.289</td>
<td>.030</td>
</tr>
<tr>
<td>PTSD symptoms at t₁ (patients)</td>
<td></td>
<td></td>
<td>.208</td>
<td></td>
</tr>
<tr>
<td>Paternal age</td>
<td></td>
<td></td>
<td>.343</td>
<td>.009</td>
</tr>
</tbody>
</table>

* p<.05; ** p<.01

1PSS-R sum-scores were logarithmically transformed (log(sum-score+1)); R², explained variance.

Table 5. Stepwise Hierarchical Multiple Regression Analysis of depressive symptoms in partners of patients at t₂ (n=37)

<table>
<thead>
<tr>
<th></th>
<th>Adj. R²</th>
<th>Δ R²</th>
<th>Beta</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 2: Factors known at t₁ and t₂</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 1: Factors known at t₁</td>
<td></td>
<td>.546</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms at t₁ (partners)</td>
<td></td>
<td></td>
<td>.252</td>
<td>.061</td>
</tr>
<tr>
<td>PTSD symptoms at t₁ (partners)</td>
<td></td>
<td></td>
<td>.171</td>
<td>.155</td>
</tr>
<tr>
<td>Education (lower/higher)</td>
<td></td>
<td></td>
<td>.166</td>
<td>.147</td>
</tr>
<tr>
<td>Paternal age</td>
<td></td>
<td></td>
<td>.253</td>
<td>.034</td>
</tr>
<tr>
<td>Step 2: Factors known at t₂</td>
<td></td>
<td>.097</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td></td>
<td></td>
<td>-.015</td>
<td>.908</td>
</tr>
<tr>
<td>Perinatal infant death</td>
<td></td>
<td></td>
<td>.256</td>
<td>.053</td>
</tr>
<tr>
<td>Depressive symptoms at t₂ (patients)</td>
<td></td>
<td></td>
<td>.221</td>
<td>.134</td>
</tr>
</tbody>
</table>

* p<.05

1BDI-II sum-scores were logarithmically transformed (log(sum-score+1)); R², explained variance. Final step shown.

Table 5 shows the SMRA for depressive symptoms (BDI-II sum scores) of partners of patients at t₂. The model for SQRT BDI explained 55% (adjusted R²) of the variance in BDI sum scores in the first step (Sig. F change <.001) and an additional 9.7% in step 2 (Sig. F change = .023). The only significant predictor of high BDI sum-scores at t₂ was higher paternal age (table 5).
DISCUSSION

Considering that women with PE and PPROM are more prone to developing PTSD than women with uncomplicated pregnancies, the aim of this study was to investigate whether this difference was also found in their partners. We found no significant differences between partners of patients and partners of controls. On the other hand, symptoms of PTSD and depression in men and women often co-occurred at 6 weeks postpartum, which adds to the emerging evidence that fathers should not be overlooked when it comes to the psychological impact of pregnancy and childbirth.

Strengths of the study include its prospective longitudinal design, a population that has not often been researched (partners of women with pregnancy complications), and the fact that a representative group of males was willing to participate at $t_1$. Differences between partners of patients and partners of controls (table 1) were in part as expected, as more cesarean sections and a lower gestational age were found in the patient group. However, partners of controls were on average older and higher educated than partners of patients. Partners of controls also more often indicated current psychiatric treatment than partners of patients (0/37 vs. 5/29; p=.013). This discrepancy may either be due to a higher prevalence of mental health problems in this group, or fewer (personal or financial) barriers in seeking treatment. While we cannot say with certainty, the fact that partners of patients and partners of controls groups report a similar percentage of a history of depression and PTSD is indicative for a difference in treatment-seeking behavior. In all cases of current treatment, men already received treatment prior to the birth of their child for a range of indications including depression, OCD and psychosis. Contrary to expectations, psychiatric history was not strongly associated with symptoms of depression or PTSD postpartum in this study. Interestingly, older fathers reported significantly more symptoms of depression and PTSD at $t_2$ as shown in the SMRA, which is a finding that cannot easily be explained based on previous research and therefore may warrant additional investigation.

Unfortunately, the sample of partners was fairly small ($n=85$ at $t_1$ and $n=66$ at $t_2$), and partners of patients who dropped out of the study after $t_1$ had more PTSD symptoms (on average) than partners of patients who participated during both time points. Both factors may at least partially explain why no differences were found between partners of patients and partners of controls in prevalence rates and sum-scores of PTSD and depression, and they could possibly have resulted in an underestimation of prevalence rates at $t_2$. On the other hand, one could also argue that the drop-out of those with more symptoms at $t_1$ means that symptoms at $t_2$ are not merely the result of pre-existing psychopathology. One may hypothesize that, related to “avoidance” as one of the symptom categories of a PTSD diagnosis, the men with PTSD at $t_1$ declined further participation in the study because reflecting on the birth of their child and the early postpartum period was too confronting for them. Interestingly enough, both for PTSD and depression, prevalence rates are not significantly higher (or even lower) postpartum than during pregnancy. This too may be an effect of selective drop out, and it is also important to note that the $t_1$ findings should not be seen as baseline
measurements, as female patients and their partners were likely to be already stressed due to the hospitalization and imminent preterm birth. A larger study may reveal whether the trend observed in this study (more PTSD symptoms in partners of patients than in partners of controls) is found significant with a higher number of participating patients and partners. One may also consider to include baseline measurements and a longer follow-up, as we know from the literature that women may also develop PTSD later than six weeks postpartum, and the highest incidence of male postpartum depression seems to be three to six months postpartum.15

The prevalence of PTSD in partners of patients was found to be 6% at t₁ and 3% at t₂, and 0% among partners of controls both in pregnancy and postpartum. Other studies of postpartum PTSD in men found prevalence rates varying from 0 to 5%.10,19,21 In our current study, the prevalence of depression among fathers was 4% in pregnancy and 5% postpartum, which is lower than the 10% recently estimated in a large meta-analysis.19 While this may have to do with our population, it could also be due to our strict adherence to the cut-off value listed in the BDI-II manual (sum score ≥20) for moderate or severe depression.33 If we would have also included mild depression (cut-off value of 10) as many previous studies did13,48,50, the prevalence of depression in men would be 33% (partners of patients) and 12% (partners of controls) in pregnancy and 14% (partners of patients) and 7% (partners of controls) postpartum. While the benefits of the BDI have previously been mentioned, one may also consider using a questionnaire that has been specifically designed for the pregnancy and postpartum period, such as the Edinburgh Postnatal Depression Scale (EPDS).51 Even though the EPDS does not include all DSM-IV criteria, it is frequently used and has also been validated for males.52

The lower prevalence rates of PTSD and depression in men than in women found in this study are in accordance with some studies, but not in line with some other studies that found similar rates.10,13,19,21 Intuitively, one may assume that women will experience more symptoms, as (a) the lifetime prevalence rates of PTSD and depression are higher in women than in men53,54; (b) women are 2.3 times more likely to develop PTSD following a traumatic event than men55; (c) postpartum depression in men may develop following the onset of depression in women52; (d) women have actually experienced pregnancy, labor (pain) and obstetric interventions, while men have merely witnessed, and therefore effects of a different magnitude may be found. The association we found between symptoms of depression and PTSD is well known from literature.47,56 Furthermore, the strong within-couple correlation of PTSD and depression symptom severity that was observed postpartum is in line with the findings of previous research that men’s and women’s responses after childbirth are strongly interlinked in the case of PTSD14, and 24-50% of the partners of women with postpartum depression also get postpartum depression.16

Instead of solely focussing on the new mother, these findings call for a system-oriented approach, evaluating the well being of woman and partner. For future studies we would therefore recommend to always include fathers, and consider the dyad rather than individuals, as partners’ symptoms of
PTSD and depression postpartum are strongly associated. Early identification and intervention could possibly prevent families from entering a downward spiral, with potentially adverse consequences for the partner relationship and parent-infant bonding, and avoidance of future pregnancies. In summary, this study is one of the first to provide data on PTSD and depression in partners of women with severe pregnancy complications. Contrary to expectations, no differences were found in the occurrence of symptoms of PTSD and depression between partners of patients and partners of controls. Higher paternal age was associated with more symptoms of PTSD and depression in partners of patients. In both groups, we observed significant overlap between symptoms of PTSD and depression, as well as between partners.
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