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ARTICLE

Severe postpartum hemorrhage increases risk of posttraumatic stress disorder: a prospective cohort study

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ABSTRACT

Purpose: To evaluate whether severe postpartum hemorrhage (PPH) is a risk factor for posttraumatic stress disorder (PTSD). Severe PPH can be experienced as a traumatic event. PTSD leads to negative mental health effects. Knowing risk factors for PTSD during childbirth offers opportunities for early interventions, which may prevent the development of PTSD.

Materials and methods: In this prospective study, we compared two groups of participants; women with ≥2000 mL of blood loss (severe PPH, patients) and women with ≤500 mL of blood loss (controls). Participants were screened for PTSD using the PCL-5 four to six weeks after delivery. Positive screening was followed by the CAPS-5 to diagnose PTSD.

Results: We included 187 PPH patients and 121 controls. Median PCL-5 scores were higher for PPH patients (5.0) than controls (4.0, $p = 0.005$). Thirteen PPH patients (7.0%) and two controls (1.7%) scored ≥32 on the PCL-5, indicative of probable PTSD (OR 4.45, 95% CI 0.99-20.06, $p = 0.035$). Significant more PPH patients than controls met criteria for a clinical diagnosis of PTSD on the CAPS-5 ($n = 10$, 5.6% vs $n = 0$, 0.0%; $p = 0.007$).

Conclusions: There is a significant and clinically relevant increased risk for developing PTSD after severe PPH. Gynecologists and midwives are advised to screen for PTSD at postpartum follow-up visits to prevent long-term negative mental health effects.

Clinical Trial Registration: NL50273.100.14

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Posttraumatic stress disorder; severe postpartum hemorrhage; subthreshold posttraumatic stress disorder; traumatic birth

Introduction

Severe postpartum hemorrhage (PPH) is a serious complication and the leading cause of maternal deaths worldwide. Unfortunately, incidence rates are increasing [1]. According to the WHO, PPH is defined as ≥500 ml of blood loss in the first 24 h after giving birth [1]. Severe PPH of ≥2000 ml will lead to significant physical complaints and patients often describe this experience as very traumatic with high emotional impact [2,3].

Posttraumatic stress disorder (PTSD) is a trauma and stressor-related disorder that may develop in response to experiencing a traumatic event [4–6]. Symptoms of PTSD include re-experiencing, avoidance, negative alterations in cognitions and mood and hyperarousal [7]. The prevalence rate of PTSD associated with childbirth is estimated between 0.9–4.9%, [8–10] but up to half of the patients who meet criteria for PTSD remain unrecognized [11]. Known risk factors for PTSD encompassing pregnancy and childbirth can be divided into obstetric, psychological and situational factors. Examples are: history of PPH, previous trauma, depression during pregnancy, premature delivery, premature rupture of membranes, preeclampsia, assisted delivery, cesarean section, and low hemoglobin levels postpartum [2,8,12–14]. Obstetric complications and

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Supplemental data for this article can be accessed here.

interventions are a major risk factor for the development of postpartum PTSD [8]. Many studies have focused on emergency cesarean sections, assisted vaginal deliveries and prematurity [12,14,15]. Given the potential life threatening situation for the woman in case of a major postpartum hemorrhage, we hypothesized that this could potentially also be an important risk factor. However, literature supporting this hypothesis was thus far lacking [16]. The only systematic review found that all studies concerning this subject used different definitions of PPH [16]. Furthermore, in all studies different primary outcomes and different measurements to assess PTSD were used and thus no conclusions can be drawn [2,15–19]. Subthreshold PTSD (or partial, subclinical or subsyndromal PTSD) is widely defined as having symptoms of PTSD but below the threshold for diagnosis, but thus far there is no definitive definition. Subthreshold PTSD can cause negative mental health effects similar to PTSD [20,21].

If severe PPH increases the risk for developing PTSD this offers clear opportunities for prevention and early interventions. PTSD can be screened soon after the event and (online) support can be offered or patients can be referred to specialized care [22]. Treatment options include trauma-focused cognitive behavioral therapy (CBT) and eye movement desensitization and reprocessing (EMDR) [23–25]. Early screening and intervention may prevent the development of severe posttraumatic stress, potentially avoiding negative effects in both the parent and the child (i.e. problems in the child's socio-emotional, cognitive, language and brain development) [11,26,27]. Furthermore, symptoms of PTSD can overlap with symptoms of postpartum depression (PPD) and thus PPD can be wrongly diagnosed [28].

This is the first study to have used a viable and severe cutoff for postpartum hemorrhage. Also, in contrast to previous research, this study uses the golden standard for screening and clinically diagnosing PTSD according to the DSM-5.

The purpose of this study was to answer if severe PPH is a risk factor for developing PTSD.

Materials and methods

In this multicenter prospective cohort study (IPAD-study; Identification of PArents in Distress), we compared patients with severe PPH ($\geq$2000 ml of blood loss) to controls ($\leq$500 ml of blood loss). We performed the same prospective cohort study with partners of patients which is published elsewhere [29]. Participants were recruited from eight hospitals in the Amsterdam region, the Netherlands. Two tertiary (university) hospitals and six secondary (general) hospitals included patients and were involved in data collection (respectively Amsterdam UMC, locations University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam and OLVG East and West (previous St Lucas Andreas Hospital), Amsterdam; Spaarne Gasthuis, Haarlem and Hoofddorp; Westfriesgasthuis, Hoorn; Flevoziekenhuis, Almere). Patients were included from February 2015 until June 2017. Demographic and delivery-related data were collected from patients' hospital files. Blood loss was measured according to standardized protocols in different hospitals, with the national guideline advising to weigh the blood loss rather than estimating it. We defined a cut-off value of 2000 ml of blood loss or more because of the physical impact of such an amount of blood loss, such as experiencing tachycardia, hypotension and dizziness.

In the Netherlands, the prevalence of PTSD in the general postpartum population is 1.2% [12]. The sample size of the study was calculated using a significance level of 0.05 and power of 80%. The expected prevalence in the control group is 0.012, the expected prevalence in the PPH group 0.087 (7.5% absolute difference). This resulted in a required number of patients of 130 per group. Our study protocol has been published elsewhere [30]. Patients were not involved in the development of the trial.

The study was approved by the institutional and/or national research committee (MEC-U (Medical Research Ethics Committees United) and the Medical Ethics Committees of each participating hospital, Clinical Trial Registration: NL50273.100.14).

Procedures

A flow diagram is added to give an overview of the timeline of the study (Figure 1). If severe PPH occurred, this patient and two controls were asked to participate in the study. Controls were defined as the following and preceding birth after the patient with PPH. We selected two controls for each PPH patient because of the experience of lower inclusion rates of controls due to the fact that controls may be dismissed soon after the delivery.

Exclusion criteria were: (1) history of PTSD; (2) age $<$18; (3) language other than English or Dutch (Table 1). All participants received verbal and written information of the study and provided written informed consent.

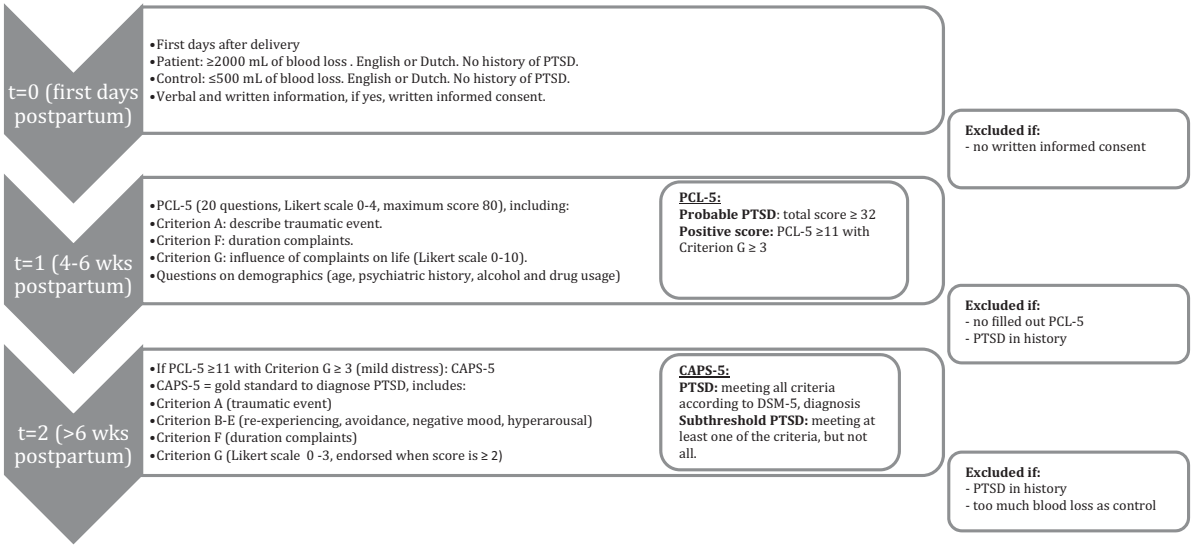

Figure 1. Flow diagram of the timeline of the study containing exclusion criteria to clarify the order of events.

Table 1. In- and exclusion criteria.

	PPH patients	Controls
Inclusion criteria	Severe PPH (≥2000 mL)*	No PPH** (≤500 mL)
	Any type of delivery	Any type of delivery
	All complications of delivery***	All complications of delivery***
	Gestational age ≥16 weeks	Gestational age ≥16 weeks
Exclusion criteria	Medical history of PTSD	Medical history of PTSD
	≤18 years	≤18 years
	Inability to speak or write Dutch	Inability to speak or write Dutch

*No matter the cause (atonia, retained placenta, coagulation disorder, rupture etc.).
**As defined by the World Health Organization (WHO).
***I.e. hypertensive disorders, congenital abnormalities, premature rupture of membranes etc.
PPH: postpartum hemorrhage, as recorded in patients' files (either estimated or weighted); PTSD: posttraumatic stress disorder.

Between four to six weeks postpartum, the digital version of the PCL-5 was sent to all participants to screen for probable PTSD. Positive screening on the PCL-5 was followed by the CAPS-5 for diagnosis of (subthreshold) PTSD.

Assessment of probable PTSD

The PCL-5 is a 20-item self-report tool that assesses the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) symptoms of PTSD, namely B Criterion (re-experiencing), C Criterion (avoidance), D Criterion (negative alterations in cognitions and mood) and E Criterion (hyperarousal) [7,31]. Respondents indicated how much they have been bothered by each PTSD symptom in the past month on a five-point Likert scale, ranging from 0–4. In the PCL-5, a score of ≥32 is indicative of probable PTSD (Figure 1) [7,31,32]. The maximum score of the PCL-5 is 80.

Questions were added in the digital questionnaire alongside the PCL-5 to explore the traumatic event (Criterion A), duration (Criterion F), functional significance (Criterion G, eleven-point Likert Scale, 0–10), co-morbidities, participants' search for treatment, depression, and use of antidepressant medication during pregnancy (Online Appendix 1).

It was not feasible to conduct the CAPS-5 with all participants, and thus, prior to the study, we excluded participants with low symptom levels on the PCL-5 who were unlikely to meet criteria for a PTSD diagnosis according to the CAPS-5. To be included, a sensitive-based cutoff was set, using a PCL-5 score of ≥11, with a self-reported severity score of ≥3 (ranging 0–10), as to not miss any participants with potential (subthreshold) PTSD.

Assessment of (subthreshold) PTSD

Participants with positive screening on the PCL-5, were asked to participate in a telephone interview in which the CAPS-5 questionnaire was administered. We conducted telephone interviews to increase the

participation and response rate. It is known that patients with PTSD avoid situations or places that may trigger flashbacks, such as hospitals. Also, young parents have less time and energy to participate in an extensive clinical interview.

The CAPS-5 is the gold standard for diagnosing PTSD and is a 30-item structured interview [33]. In addition to assessing the DSM-5 PTSD symptoms, questions target the onset and duration of symptoms, subjective distress, impact of symptoms on social and occupational functioning, overall response validity, overall PTSD severity, and specifications for the dissociative subtype [31,34–36]. PTSD was diagnosed when a participant scores at least one B Criterion, one C Criterion, two D Criterion, two E Criterion, and when Criterion F and G are met [33,35], according to DSM-5. The assessor combines information about the intensity and frequency of each item and scored accordingly. Clinical researchers were officially trained to conduct the CAPS-5. Blind assessment was not possible, due to the fact that Criterion A had to be known to conduct the CAPS-5.

Outcome measures

Our primary outcome measures were: probable PTSD, diagnosis of PTSD and subthreshold PTSD. Probable PTSD was diagnosed when a participant scored $\geq$32 on the PCL-5.

PTSD was diagnosed when a participant met the DSM-5 criteria according to the CAPS-5 (Figure 1), or when PTSD was clinically diagnosed postpartum and treated by a psychiatrist or psychologist (as indicated by the participants).

Participants met criteria for subthreshold PTSD when a participant met at least one of the abovementioned criteria for PTSD according to the CAPS-5, but not all, in combination with a Criterion G score of $\geq$2 (Figure 1).

When the CAPS-5 interview revealed a history of PTSD, participants were excluded from participation. Participants were also excluded when other exclusion criteria were met, even if the PCL-5 had already been completed (Figure 1). When PTSD was diagnosed, participants were referred to their general practitioner, who arranged further referral to a specialized psychologist, which is standard procedure in the Netherlands.

Statistical analysis

The primary outcome of this study was whether severe PPH is a risk factor for developing PTSD. Dichotomous data were compared using Chi-square analysis (χ^2) or Fisher's exact test where applicable. Continuous data were compared either with *t*-tests or Mann-Whitney U tests. All tests were two-tailed and $p < 0.05$ denoted significance. Bonferroni correction was not performed since this is an explorative study and there was a restricted number of planned comparisons [37]. Data were analyzed using the Statistical Package for the Social Sciences (SPSS, Version 22).

Multivariable logistic regression analysis as foreseen in the protocol paper was not possible due to the small number of participants with PTSD [30]. Therefore, univariable logistic regression was used for the association between the known risk factors for PTSD (history of PPH, depression during pregnancy, premature delivery, premature rupture of membranes, preeclampsia, assisted delivery, and cesarean section). Since the postpartum hemoglobin levels were not known in most of the controls, we could not perform any analyses with this variable. These univariable logistic regression analyses were performed with the data of the participants (PPH patients and controls) who were diagnosed with PTSD in our study combined with the data of the participants diagnosed with PTSD by a psychologist, but who did not want to have the CAPS-5 administered ($n = 13$). The remaining 12 participants (eight PPH patients and four controls) who were lost to follow up after the PCL-5 and did not disclose whether they were diagnosed with and treated for PTSD, were excluded in these analyses.

Results

Baseline characteristics

We received a total of 270 informed consents from PPH patients and 176 from controls. The PCL-5 was completed by 70.4% ($n = 190$) of the PPH patients and 74.4% ($n = 131$) of the controls. Of these participants, three PPH patients and ten controls had to be excluded based on the exclusion criteria (PTSD in their history or too much blood loss in controls). Accordingly, the data of 187 PPH patients and 121 controls were analyzed (Figure 2(a,b)).

Table 2 presents an overview of the baseline characteristics of the participants. Primiparity (54.5% vs 66.1%), mean birthweight (3563 grams vs 3332 grams), pain relief during delivery (43.3% vs 57.0%), history of PPH (15.5% vs 3.3%), average duration of third stage of labor (45 min vs 9 min) and average duration of hospitalization (3 vs 2 days) differed significantly between PPH patients and controls. Shortest duration of pregnancy was 31 + 5 weeks. Baseline characteristics

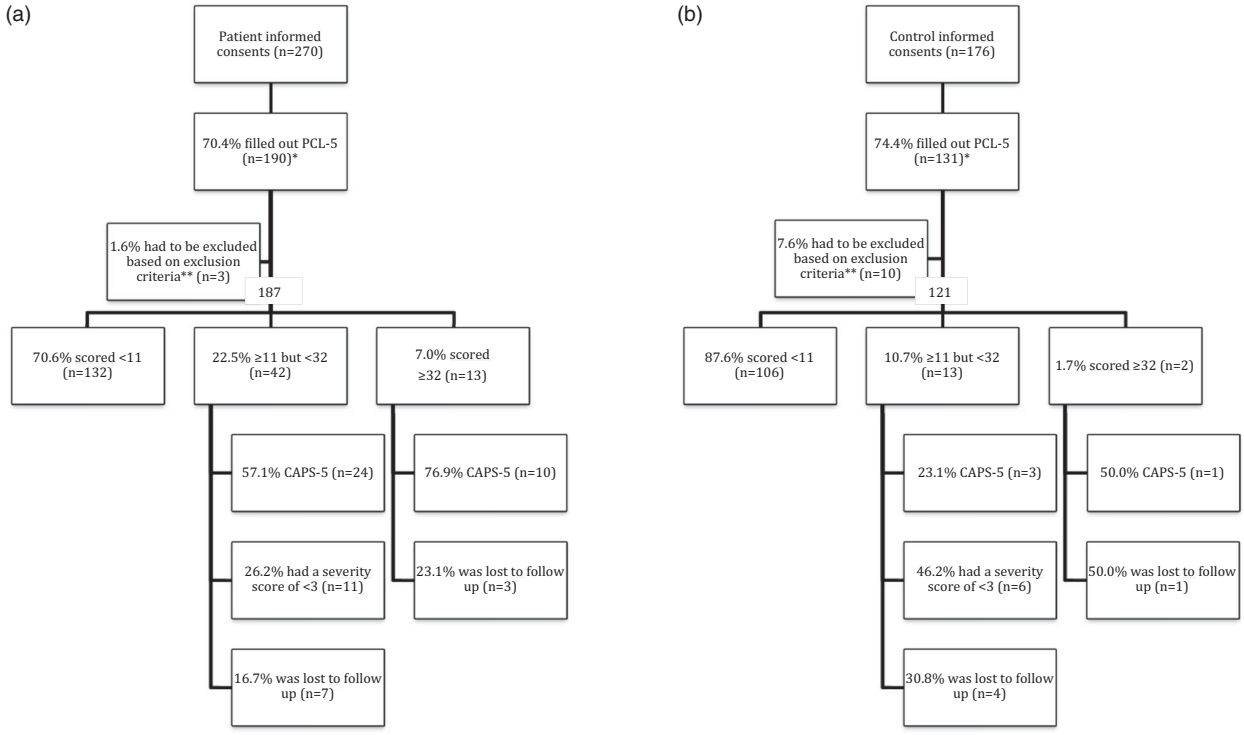

Figure 2. (a,b) Flowchart of the inclusions in our study. *Everyone was sent the PCL-5, but not everyone filled it out. **Exclusion criteria consisted of PTSD in history and ≤500 mL of blood loss (controls). PCL-5: PTSD Checklist for DSM-5; CAPS-5: Clinician-Administered PTSD Scale for DSM-5; PTSD: posttraumatic stress disorder.

Table 2. Baseline characteristics.

Characteristics	PPH patients (blood loss ≥ 2000 mL) ($n = 187$)	Controls (blood loss ≤ 500 mL) ($n = 121$)	p Value
Age, years	32.7 ± 4.2	32.6 ± 4.2	0.720
Completed college or university*	135 (73.8)	88 (72.7)	0.840
BMI*	23.5 ± 4.4	23.3 ± 3.8	0.640
Reported history of depression	11 (5.9)	9 (7.4)	0.588
Primipara[a]	102 (54.5)	80 (66.1)	0.044
Gestational age, week + day*	40 + 1 (38 + 6–41 + 0)	39 + 4 (38 + 1–40 + 6)	0.083
Birth weight, grams[a,*]	3563 ± 578	3332 ± 583	0.001
Spontaneous start of delivery	97 (51.9)	56 (46.3)	0.338
Pain relief during delivery[a]	81 (43.3)	69 (57.0)	0.019
Vaginal delivery	144 (77.0)	87 (71.9)	0.312
Ventouse delivery	18 (9.6)	14 (11.6)	0.585
Planned cesarean	14 (7.5)	5 (4.1)	0.232
Emergency cesarean	11 (5.9)	14 (11.6)	0.074
Assisted delivery	43 (23.0)	33 (27.3)	0.395
History of PPH[a,+]	29 (15.5)	4 (3.3)	0.001
Blood loss, mL[a]	2500 (2000 – 3000)	300 (200 – 400)	<0.001
Delivered during shift[+++]	106 (57.3)	67 (56.3)	0.864
Third stage of labor, minutes[a,*]	45 (8 – 80)	9 (5 – 15)	<0.001
Received packed cells[a]	114 (61.0)	0 (0.0)	<0.001
Hospitalization of mother, days[a,*]	3 (2 – 4)	2 (1 – 3)	<0.001
Feeling bleeding to death[a,++]	92 (49.2)	6 (5.0)	<0.001
Time between delivery and PCL-5, days*	51 (41 – 65)	48 (39 – 68)	0.407
Time between delivery and CAPS-5, days*	82 (65 – 111)	120 (97 – 127)	0.098

All variables are shown in n (%), mean ± SD or median (25–75%). All differences were analyzed using χ^2, t-test or Mann-Whitney U, except if stated otherwise below.

[a]Significant difference between patient group and control group.

[+]History of PPH: defined according to the Dutch Society of Obstetrics and Gynecology (NVOG): ≥1000 ml of blood loss after a vaginal or instrumental delivery.

[++]Feeling bleeding to death: as answered by patients in the digital questionnaires. Affirmative answers were: a little bit, moderately, a lot, extremely.

[+++]Delivered during shift: all deliveries between 17:00 and 08:00.

[*]Due to incomplete data, measurements were based on: completed college or university PPH patients $n = 183$, controls $n = 121$; BMI PPH patients $n = 175$, controls $n = 113$; birth weight PPH patients $n = 180$, controls $n = 120$; delivered during shift PPH patients $n = 185$, controls $n = 119$; third stage of labor PPH patients $n = 179$, controls $n = 116$; days of admission PPH patients $n = 185$, controls $n = 121$; days between delivery and CAPS-5 PPH patients $n = 35$, controls $n = 5$.

BMI: body mass index; PPH: postpartum hemorrhage; PCL-5: PTSD Checklist for DSM-5; CAPS-5: Clinical Administered PTSD Scale for DSM-5.

were comparable with the whole group who gave informed consent (Supporting information–Table 1).

PCL-5 and CAPS-5

In total, 22.5% of PPH patients ($n = 42$) and 10.7% of the controls ($n = 13$) scored between 11 and 32 on the PCL-5. Seven percent of PPH patients ($n = 13$) and 1.7% of the controls ($n = 2$)) scored ≥32, indicative of probable PTSD (unadjusted odds ratio (OR) 4.45, 95% confidence interval (CI) 0.99–20.06; Table 3), the calculated p value ($p = 0.035$) did show a significant difference. Median PCL-5 scores were higher for PPH patients (5.0) than controls (4.0, $p = 0.005$).

Because we only administered the CAPS-5 when the self-report severity score (Criterion G) was three or more, 20.0% of PPH patients (11 out of 55) and 40.0% of the controls (6 out of 15) were not invited for an additional CAPS-5 interview (Figure 2(a,b)). Seven PPH patients with a PCL-5 score ≥11 and three PPH patients with a PCL-5 score ≥32 were lost to follow up. In the control group, four controls with a PCL-5 score ≥11 and one control with a PCL-5 score ≥32 were lost to follow up. Reasons for loss to follow up were unwillingness to participate any longer or by being unreachable. Three of these participants (two PPH patients and one control) who did not want to participate any longer after filling out the PCL-5, but who did give informed consent, disclosed they were diagnosed with PTSD after delivery and that they were being treated. Eventually, this resulted in the administration of 34 out of 44 (77.3%) CAPS-5 interviews in the PPH patient group, and in 4 out of 9 (44.4%) CAPS-5 interviews in the control group (Figure 2(a,b)).

The prevalence of PTSD according to the CAPS-5 in the PPH patient group was 5.6% ($n = 10$), which was significantly different compared to the control group at 0.0% ($n = 0$, $p = 0.007$; Table 3). When also taking into account the participants who disclosed they were diagnosed with PTSD postpartum (but who did not want to participate in the CAPS-5 interview), 6.7% ($n = 12$) of the PPH patient group and 0.9% ($n = 1$) of the control group met criteria for PTSD (OR 8.34, 95% CI 1.07–64.99; Table 3).

Subthreshold PTSD alone was not significantly associated with PPH with 4.5% ($n = 8$) in the PPH patient group and 0.9% in the control group ($n = 1$, OR 5.44, 95% CI 0.67–44.11; Table 3). The two controls with subthreshold PTSD or PTSD (according to a psychologist) reported a feeling of bleeding to death postpartum, even though they both had 400 ml of blood loss.

Figure 3 shows that PPH patients and controls with PTSD scored relatively highly on Criterion B (reexperiencing). The mean score of Criterion B was 3.5 (with a minimum score of 1 and a maximum score of 5).

The relationship between the amount of blood loss and the development of PTSD within the PPH patient group (≥2000 ml blood loss) was analyzed by comparing the median amount of blood loss in the PPH patient group *with* PTSD ($n = 12$) and the PPH patient group *without* PTSD ($n = 167$). We found no significant

Table 3. Outcomes PCL-5 and CAPS-5.

PCL-5 and CAPS-5 results	PPH patients (blood loss ≥ 2000 mL) ($n = 187$)	Controls (blood loss ≤ 500 mL) ($n = 121$)	Unadjusted OR (95% CI)	p Value
PCL-5, median score[a]	5.0 (2.0 − 12.0)	4.0 (1.0 − 7.0)	N/A	0.005
PCL-5, score ≥11[a]	55 (29.4)	15 (12.4)	2.94 (1.58-5.50)	0.001
PCL-5, score ≥32, probable PTSD[a]	13 (7.0)	2 (1.7)	4.45 (0.99-20.06)	0.035
CAPS-5, PTSD[a,*,+,1]	10 (5.6)	0 (0.0)	N/A	0.007
Clinically diagnosed PTSD no CAPS-5[+]	2 (1.1)	1 (0.9)	N/A	N/A
PTSD total, CAPS-5 + clinically diagnosed[a,+]	12 (6.7)	1 (0.9)	8.34 (1.07-64.99)	0.016
CAPS-5, subthreshold PTSD[*,+]	8 (4.5)	1 (0.9)	5.44 (0.67-44.11)	0.093
CAPS-5, reeexperiencing[++]	1.8 ± 1.6	0.8 ± 1.5	1.69 (0.72-4.00)	0.211
CAPS-5, avoidance[++,a]	0.6 ± 0.7	0.0 ± 0.0	N/A	<0.001
CAPS-5, negative mood[++]	1.7 ± 1.9	0.5 ± 1.0	1.83 (0.63-5.36)	0.227
CAPS-5, hyperarousal[++]	1.5 ± 1.5	0.8 ± 1.5	1.47 (0.62-3.51)	0.381
CAPS-5, functional significance[++]	1.4 ± 1.2	0.8 ± 1.5	1.63 (0.62-4.30)	0.318
CAPS-5, dissociative symptoms[++]	3 (8.6)	0 (0.0)	N/A	N/A

All variables are shown in n (%), mean ± SD or median (25-75%). All differences were analyzed using χ^2, t-test or Mann-Whitney U, except if stated otherwise below.

[a]Significant difference between PPH patient group and control group.

[*]Fisher's exact test.

[+]Due to incomplete data, measurements were based on: subthreshold PTSD PPH patients $n = 177$, controls $n = 116$; PTSD according to CAPS-5 PPH patients $n = 177$, controls $n = 116$; clinically diagnosed PTSD PPH patients $n = 179$, controls $n = 117$; PTSD total including clinically diagnosed PPH patients $n = 179$, controls $n = 117$; subthreshold PTSD PPH patients $n = 179$, controls $n = 117$.

[++]Administered CAPS-5 PPH patients $n = 34$, controls $n = 4$.

[1]No OR since the control group has 0.0% PTSD.

OR: odds ratio; CI: confidence interval; N/A: not applicable; PCL-5: PTSD Checklist for DSM-5; CAPS-5: Clinical Administered PTSD Scale for DSM-5; PTSD: posttraumatic stress disorder; PPH: postpartum hemorrhage.

difference between the median amount of blood loss in the PPH patient group *with* PTSD (2500 ml (2000–3750 ml)) and the PPH patient group *without* PTSD (2500 ml (2000–3000 ml), Mann-Whitney U test ($p = 0.754$)); Figure 4).

Other risk factors for developing PTSD

Univariable logistic regression analyses showed a significant association between premature delivery (OR 4.21, 95% CI 1.22–14.60) and PTSD. The other known risk factors were not significantly associated with PTSD (Table 4).

Even though pain relief, duration of third stage of labor, primiparity, birthweight and duration of hospitalization were significantly different between PPH patients and controls according to baseline characteristics, no significant association between pain relief, duration of third stage of labor, primiparity and PTSD was observed. Birthweight and duration of hospitalization showed a significant difference between participants with and without PTSD (Table 4).

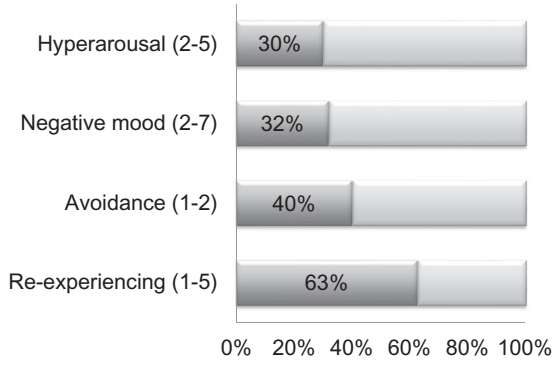

Figure 3. Relative scores of PTSD criteria B-E on a range of 0–100%. Minimum and maximum values stated after the Criteria. Criterion B: re-experiencing, Criterion C: avoidance, Criterion D: negative mood, Criterion E: hyperarousal.

Discussion

In this study we examined whether severe PPH is a risk factor for developing PTSD or subthreshold PTSD. The PCL-5, which we used as a screening test, showed a significantly higher median score in PPH patients. There were significantly more PPH patients scoring above the cutoff for probable PTSD.

The CAPS-5, conducted in 34 of the 187 PPH patients and four of the 121 controls, showed that significantly more PPH patients than controls met the criteria for PTSD diagnosis based on the CAPS-5. Subthreshold PTSD was not significantly associated with severe PPH.

Previous studies evaluating PTSD after PPH showed inconsistent results. Our findings are in line with a

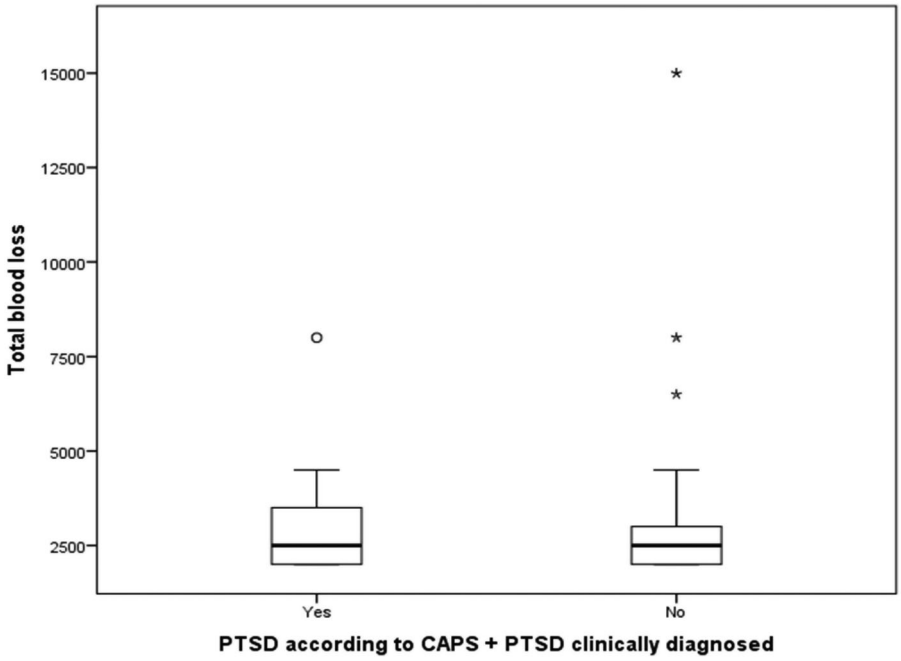

Figure 4. Median blood loss in PPH patients with PTSD and without PTSD. Comparison in median amount of blood loss between PPH patients with PTSD and PPH patients without PTSD (control group excluded). Median amount of blood loss in PPH patients with PTSD: 2500 mL (2000–3750 mL). Median amount of blood loss in PPH patients without PTSD: 2500 mL (2000–3000 mL). PTSD: posttraumatic stress disorder.

Table 4. Univariable regression analyses with known risk factors and baseline characteristics that are significantly different.

	PTSD total[1] ($n = 13$)	No PTSD ($n = 283$)	Unadjusted OR (95% CI)	p Value
History of PPH[+,**]	2 (15.4)	29 (10.2)	1.59 (0.34–7.54)	0.634
Depression during pregnancy[**]	0 (0.0)	1 (0.4)	N/A	1.000
Premature delivery[a,**]	4 (30.8)	27 (9.5)	4.21 (1.22–14.60)	0.036
Premature rupture of membranes[**]	1 (7.7)	7 (2.5)	3.29 (0.374–28.88)	0.305
Preeclampsia[**]	1 (7.7)	9 (3.2)	2.54 (0.30–21.68)	0.366
Assisted delivery (vaginal or surgical)[**]	3 (23.1)	68 (24.0)	0.95 (0.25–3.55)	1.000
Cesarean section (elective and emergency)[**]	2 (15.4)	39 (13.8)	0.88 (0.19–4.12)	0.698
Pain relief	6 (46.2)	135 (47.7)	0.94 (0.31–2.87)	0.913
Third stage of labor, minutes[*]	8 (4−104)	14 (7−59)	N/A	0.944
Primipara	5 (38.5)	172 (60.8)	0.40 (0.13–1.26)	0.109
Birth weight, grams[a,*]	3111 ± 633	3494 ± 588	0.37 (0.16–0.89)	0.023
Days of hospitalization[a]	3.0 (2.5−5.0)	3.0 (2.0−3.0)	N/A	0.040

All variables are shown in n (%), mean ± SD or median (25-75%). All differences were analyzed using χ^2, *t*-test or Mann-Whitney U, except if stated otherwise below.
[a]Significant difference between PTSD and no PTSD.
[+]History of PPH is defined as having a previous delivery complicated by PPH (≥1000 ml).
[*]Due to incomplete data, measurements were based on: third stage of labor PTSD total $n = 12$, no PTSD $n = 272$; birth weight PTSD total, $n = 13$, no PTSD $n = 275$; days of hospitalization PTSD total = 13, no PTSD = 281.
[**]Fisher's exact test.
[1]PTSD according to CAPS-5 + clinically diagnosed.
OR: odds ratio; CI: confidence interval; PPH: postpartum hemorrhage; PTSD: posttraumatic stress disorder; CAPS-5: Clinical Administered PTSD Scale for DSM-5.

retrospective study by Stramrood et al. [15] who found a significant association between PPH (≥1000 ml) and PTSD in their univariable analysis and with the pilot study of Ricbourg *et al.*, [19] who found a significant association between PPH and PTSD one month postpartum. Three studies on this subject did not find an association between PPH and PTSD, but they all defined PPH differently and not one study defined severe PPH as more than 2000 ml of blood loss [2,17,18]. This may explain the difference in outcomes between these three studies and our results. One can imagine that the physical and consequential impact of ≥2000 ml of blood loss postpartum is different than a 500 − 2000 ml blood loss, since ≥2000 ml will likely cause physical complaints.

Another possible explanation for the inconsistent results of the previous studies is that PTSD was assessed differently in all five studies, using various measurements (Impact of Event Scale - Revised (IES-R), Traumatic Event Scale (TES) and the PTSD Checklist (PCL)) [16]. Furthermore, these measurements can only be used as screening tools, [16] whereas, to our knowledge, this is the first study that used the CAPS-5, which is the gold standard for diagnosing PTSD. In addition, most studies had a retrospective design in contrast to this prospective cohort study [16].

We found less participants with subthreshold PTSD than PTSD, contrarily to what is to be expected. This could be due to a too small sample size. Since subthreshold PTSD can cause similar complaints as PTSD, more research is needed [20,21].

Because multivariable analyses were not possible due to the small sample with PTSD, we performed univariable analyses with the known risk factors of PTSD surrounding delivery [2,8,12]. Only premature delivery was associated with PTSD, which is in line with the findings of the prospective study of Stramrood et al. [12]. However, it should be noted that these univariable analyses are highly biased because of the small number of participants with PTSD.

Our patient and control group did differ slightly in baseline characteristics, where the higher percentage of pain relief, lower birthweight and the shorter third stage of labor in the control group are the most striking. Previous research has shown that experiencing less pain during a traumatic event will less likely cause PTSD compared to experiencing more pain [38]. However, our univariable analyses did not show a significant association between having had pain relief and PTSD. Higher birthweight is known to be a risk factor for developing PPH, despite that, the average birthweight was lower in the PTSD group compared to the group without PTSD [39]. This is probably due to the fact that premature delivery was more prevalent in the PTSD group. Participants with longer hospitalization after delivery had significantly more PTSD, which may be explained by the fact that women who went home faster may be more resilient in coping with adverse events. This increased hospital stay may generate a time window for proactive treatment. Previous research has shown that cesarean section gives an increased risk of developing PTSD, [14]

however, we could not confirm this statement in our study.

One of the main strengths of this study is its prospective design. We included participants in the first few days after their delivery and sent the questionnaire several weeks later. Another strength is the follow-up with the CAPS-5 after an elevated score on the PCL-5, and therefore being the first study using the CAPS-5. The PCL-5 was used as a self-report screening measurement for symptoms of PTSD while the CAPS-5 is the gold standard for diagnosing PTSD. The CAPS-5 was administered (by trained clinicians) only when a participant scored $\geq$11 on the PCL-5. This cutoff value to administer the CAPS-5 was purposefully low and thus sensitive in order to not miss any participants with subthreshold PTSD. Also, we used a telephone interview, in order to lower the threshold for participation. We estimate that using this method has given a higher response rate and thus a more realistic prevalence rate, but it cannot completely be ruled out that this is still an underestimation.

The calculated sample size was not reached in the control group, which is our main limitation. This is due to the fact that more controls than expected had to be excluded based on predefined exclusion criteria after the participants already filled out the PCL-5. However, increasing the amount of participants in the control group would probably have made the difference between PPH patients and controls even more prominent. Furthermore, the study was overpowered for the PPH patient group, causing the smaller than anticipated difference to be significant. Another limitation is the insufficient power to perform a multivariable regression analysis. Furthermore, a little over 30% of the participants (83 PPH patients (30.7%) and 45 controls (25.6%)) did not complete the PCL-5 even though we tried to contact them several times. After filling out the PCL-5, ten PPH patients (22.7%) and five controls (55.6%) were lost to follow-up and the CAPS-5 could not be administered. Because avoidance is one of the criteria of PTSD, we assume our prevalence rate is an underestimation of the real prevalence rate. Administering the CAPS-5 by telephone may have been a limitation, since it might be easier for participants to hide part of their emotions.

In conclusion, there is a significant and clinically relevant increased risk for developing PTSD after severe PPH.

Based on the findings in our study, we advise clinicians to be aware of PTSD after severe PPH and to screen patients at their postpartum follow-up, for example routinely after $\geq$ 2000 ml of blood loss or with combined risk factors. This could be done with the PCL-5. This is particularly important because symptoms can be confused with and/or overlap with PPD. It is known that early screening and intervention (e.g. online, CBT, EMDR) may prevent the development of PTSD as well as long-term health effects and economic and social problems [11,23,26,40]. When severe PPH occurs this offers a unique moment in time to identify persons at risk for posttraumatic stress reactions and to address this in the follow-up visit.

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The authors report no conflicts of interest.

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Data availability

Data are available to readers without undue qualifications in material transfer agreements

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