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Rehospitalization of Postpartum Depression and Psychosis After Electroconvulsive Therapy A Population-Based Study With a Matched Control Group

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Objectives: Electroconvulsive therapy (ECT) is used in some cases of postpartum depression (PPD) and postpartum psychosis (PPP). The risk of relapse for PPD and PPP after ECT is unknown. This study compared the relapse rate after ECT between women who had been treated for PPD and/or PPP and women who had been treated for depression and/or psychosis outside the postpartum period.

Methods: The Swedish National Quality Register for ECT and the Swedish National Patient Register were used to identify women with PPD and/or PPP who had been treated with ECT within 6 months after delivery. For each case, a control (treated with ECT but not postpartum) patient was also selected. A Kaplan-Meier estimator was used to calculate the relapse rate (defined as rehospitalization or suicide) after ECT. Cox regression was used to identify variables associated with relapse.

Results: A total of 180 patients were included in each group. The proportions of patients who suffered relapse after 6 months, 1 year, and 2 years were 28%, 31%, and 40% for the postpartum group and 39%, 50%, and 55% for the nonpostpartum group. Treatment with benzodiazepines, several previous psychiatric admissions, and the absence of improvement after ECT were associated with relapse.

Conclusions: The risk of relapse after ECT is lower for patients with PPD and/or PPP than for patients outside the postpartum period, but the risk is nonetheless substantial in both groups.

Key Words: postpartum disorders, postpartum depression, postpartum psychosis, electroconvulsive therapy, relapse

(JECT 2019;35: 264-271)

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The study was supported by Region Örebro County. The funding source had no influence on study design; the collection, analysis, and interpretation of data; the writing of the report; or the decision to submit the manuscript for publication.

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DOI: 10.1097/YCT.0000000000000578

Postpartum Depression and Postpartum Psychosis

Postpartum depression (PPD), the depression associated with childbirth, has symptoms similar to depression at other times of life and can include irritability, anxiety, sleep disturbances, and feelings of being overwhelmed. Obsessive preoccupation with the health and the feeding of the baby can also occur. Postpartum depression is more severe than the transient depressive symptoms observed in "postpartum blues," which is a common condition that can arise shortly after childbirth.² The prevalence of PPD in women after delivery is 6.5% to 12.9%.1

Postpartum psychosis (PPP) is not as common as PPD and appears in approximately 0.25 to 0.6 per 1000 deliveries.³ Postpartum psychosis can include a broad range of symptoms, including mania or mixed episodes (with or without psychotic features), depressive episodes with psychotic features, and nonaffective psychotic episodes. The onset of the symptoms usually occurs within the first weeks after delivery, but the risk of PPP can persist for a few months.3

Classifications of mental disorders associated with childbirth differ. According to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10), the onset of the symptoms for PPD and PPP occurs within 6 weeks after childbirth. 4 The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition does not include a definition of PPD or PPD but instead defines peripartum depression, whereby depression is classified as peripartum if the symptoms begin during the pregnancy or within 4 weeks after childbirth. Several studies suggest that the increased risk of postpartum mental disorders persists for at least 6 months after delivery. 6-8

Maternal depression can negatively affect mother-child interactions. This is a risk factor for developmental impairments, and it can cause disturbances in personality development, language development, and general cognitive development in infants. An increased risk of child malnutrition has also been associated with PPD. 10,11 While infanticide is uncommon, it is nonetheless a potential consequence of peripartum-onset mood episodes and has been most often associated with PPP.⁵

Although PPD and PPP can be treated, there is risk of relapse/recurrence, and the disorders are associated with an increased risk of suicide, a common cause of death in connection

The readmission rate for psychiatric disorders after PPP is high. The risk of nonpuerperal relapse/recurrence is increased several years after the psychosis, even though the risk gradually decreases with time.1

Time to relapse/recurrence in major depressive disorder decreases with the number of previous episodes and the severity of the disease. Young age is also a risk factor. ¹⁴

The first month after delivery is associated with an increased risk of relapse/recurrence. Women with bipolar disorder have a particularly high risk of postpartum episodes. 15 Therefore, the prognosis of severe affective episodes in this period is of special interest.

Electroconvulsive therapy (ECT) is used to treat PPD and PPP in some cases, such as in women with severe depression who have not responded to medications, have experienced an episode of acute psychosis, and/or who are suicidal. 16,17

The response rate to ECT is high. For severe depression, the treatment is often more effective than pharmacotherapies. In an earlier report from the same cohort, we showed that the response rate to ECT is increased in the postpartum period. 18 The much debated adverse effect of ECT is memory disturbance, which can be both anterograde and retrograde. This is a temporary adverse effect that usually does not persist for longer than a few days after treatment.15

Several studies showed a high relapse rate in depression years after ECT, 20,21 but there is a lack information on risk of relapse for PPD and PPP specifically after ECT.²² Therefore, the aim for this study was to compare the relapse rates (defined as rehospitalization or suicide) after ECT between women who had been treated for PPD and/or PPP and women who had been treated for depression and/or psychosis outside the postpartum period.

MATERIALS AND METHODS

Study Design

This study was a register-based, case-control study. Women with PPD and/or PPP who had been treated with ECT within 6 months after delivery were identified from the Swedish national quality register for ECT (Q-ECT) and the Swedish National Patient Register. A 6-month period was chosen considering findings that an increased risk of depression continues for 6 months after delivery.^{6–8} For each case, a control was selected. The controls were women who were treated with ECT for depression and/or psychosis outside the postpartum period.

Data Sources

Personal identity numbers were used to cross-link data from the O-ECT, the Swedish National Patient Register, the Swedish Prescribed Drug Register, the Longitudinal Integration Database for Health Insurance and Labour Market Studies, and the Swedish Causes of Death Register. Since 2011, the Q-ECT has been a national register that contains information on ECT treatment in Sweden.²³ Details of the ECT, the diagnoses (*ICD-10* codes), and data on depression symptoms prior to ECT according to Montgomery-Åsberg Depression Rating Scale—Self-assessment (MADRS-S)²⁴ and improvement according to the Clinical Global Impression-Improvement Scale (CGI-I) were collected from the Q-ECT. The CGI-I is a 7-point scale that measures how much a patient's condition has improved or worsened since the initiation of treatment, whereby a score of 1 indicates "very much improved," and 7 indicates "very much worsened." The Swedish National Patient Register is a mandatory register of all public and private hospital admissions in Sweden.²⁶ Hospitalizations, comorbid diagnoses, and birth dates were collected from the Swedish National Patient Register. The Swedish Prescribed Drug Register records all the prescribed medicines that are collected from a pharmacy for outpatient use.²⁷ The Swedish Causes of Death Register contains data on dates and causes of death of all deceased residents in Sweden since 1961.²⁸ The Longitudinal Integration Database for Health Insurance and Labour Market Studies contains information on education, marital status, and employment status for all citizens older than 15 years in Sweden.²⁹

Study Population—Inclusion and Exclusion Criteria

Inclusion of patients in the case group required them to have received ECT for PPD and/or PPP within 6 months after delivery. For depression without psychosis (PPD), the indication for ECT had to be one of the following ICD-10 codes: F31.3-4, F32.1-2, F32.9, F33.1-2, F33.9, or F53.0. For PPP, the indication for ECT had to be one of the following ICD-10 codes: F23.0, F23.9, F29.9, F31.5, F32.3, F33.3, or F53.1. Patients with missing CGI-I score were excluded. Patients who had not finished their ECT treatments before December 31, 2016, were also excluded, because the follow-up was limited to December 31, 2016.

The control subjects were chosen from 4248 possible women younger than 46 years who, before 2017, were treated with ECT for a nonpostpartum indication and registered in the Q-ECT. The matching of the cases and controls was performed in the following order: ECT indication (F32.2 and F33.2 [severe depression] matched with F53.0 [PPD], and F32.3 and F33.3 [severe depression with psychosis] matched with F53.1 [PPP]), the Clinical Global Impression-Severity Scale (CGI-S) score²⁵ before ECT, duration of treatment with antidepressants, and age. The matching of the main diagnosis was balanced so that the number of patients with psychosis was the same in the case and control groups. Each case was compared with 1 control only.

Outcome Measure (Relapse)

The outcome, relapse, was defined as rehospitalization for psychiatric disorder (ICD chapter F) or suicide. Rehospitalization was identified via the Swedish National Patient Register. Suicide was identified via the Swedish Causes of Death Register. Relapse (symptoms deterioration within 6 months) is frequently separated from recurrence (new episodes after the 6-month period). However, in this study, we used the term "relapse" for all rehospitalizations and suicides.

ECT Treatment

The ECT devices used were either Mecta (Mecta Corp, Lake Oswego, Ore) or Thymatron (Somatic, Lake Bluff, Ill). During the treatment, the patients were sedated with propofol or thiopenthal. The electrodes were placed unilaterally, bitemporally, or bifrontally. Details about the ECT were published previously. 18

Ethics

This study was approved by the Regional Ethical Vetting Board in Uppsala (registration no. 2014/174). Because this was a register-based study, the patients were not informed of this study, and informed consent was waived.

Statistical Analyses

Data management was performed using SAS 6.1 (SAS Institute Inc, Cary, NC). SPSS Statistics 22 (SPSS Inc, Chicago, Ill) was used for all statistical analyses. Categorical data were compared using χ^2 tests when the number of expected observations in any cell was 5 or more, and using Fisher exact test when the number of expected observations in any cell was fewer than 5. A Kaplan-Meier estimator was used to calculate the relapse rate after ECT. Cox regression was used to identify variables associated with relapse. Both univariate and multivariate analyses were performed. Multivariate analysis was performed on variables for which there was a significant difference between the case group and control group and on variables for which statistically

TABLE 1. Baseline Characteristics of the Cases and Controls

	Cases, n (%)	Controls, n (%)	P
Total	180 (100)	180 (100)	
Age at treatment start, y			
16–25	35 (19)	44 (24)	0.098
26–30	67 (37)	56 (31)	
31–35	45 (25)	33 (18)	
36–45	33 (18)	47 (26)	
Marital status			0.054
Married/cohabiting	61 (34)	48 (27)	
Divorced	5 (3)	16 (9)	
Unmarried	113 (63)	114 (63)	
No data	1 (0.6)	2(1)	
Living alone	` '	. ,	0.836
Yes	69 (38)	70 (39)	
No	110 (61)	108 (60)	
No data	1 (0.6)	2(1)	
Children	` /	. ,	0.016
Yes	180 (100)	109 (61)	
No	0 (0)	71 (39)	
Education level		,	0.004
Less than high school	31 (17)	36 (20)	
High school	54 (30)	82 (46)	
College	90 (50)	58 (32)	
Employment status	()		0.025
Employed	142 (79)	119 (66)	
Unemployed	37 (21)	59 (33)	
No data	1 (0.6)	2(1)	
Diagnosis	- (***)	= (-)	0.000
F32.1, F33.1 Moderate depression	11 (6)	12 (7)	
F32.2, F33.2 Severe depression	32 (18)	65 (36)	
F32.3, F33.3 Severe depression with psychosis	15 (8)	64 (36)	
F32.9, F33.9 Depression, unspecified	14 (8)	12 (7)	
F31.3 Bipolar affective disorder, mild or moderate depression	3 (2)	3 (2)	
F31.4 Bipolar affective disorder, severe depression without psychotic symptoms	4 (2)	5 (3)	
F31.5 Bipolar affective disorder, severe depression with psychotic symptoms	5 (3)	5 (3)	
F23.0 Acute polymorphic psychotic disorder without symptoms of schizophrenia (cycloid psychosis)	2 (1)	2 (1)	
F23.9 Acute and transient psychotic disorders	3 (2)	8 (4)	
F29.9 Unspecified nonorganic psychosis	10 (6)	4 (2)	
F53.0 PPD	33 (18)	0 (0)	
F53.1 PPP	48 (27)	0 (0)	
Psychosis	` '	,	1.000
Yes	83 (46)	83 (46)	
No	97 (54)	97 (54)	
Comorbidities	· /		
Personality disorder	6 (3)	20 (11)	0.004
Substance use disorder	16 (9)	33 (18)	0.009
Anxiety disorder	25 (14)	40 (22)	0.040
Attention-deficit/hyperactivity disorder	7 (4)	14 (8)	0.115

Continued next page

TABLE 1. (Continued)

	Cases, n (%)	Controls, n (%)	P
Severity of the disease before ECT according to the CGI-S score			0.934
1 (Normal, not at all ill)	0 (0)	0 (0)	
2 (Borderline mentally ill)	0 (0)	0 (0)	
3 (Mildly ill)	0 (0)	0 (0)	
4 (Moderately ill)	19 (11)	21 (12)	
5 (Markedly ill)	73 (41)	77 (43)	
6 (Severely ill)	75 (42)	72 (40)	
7 (Among the most extremely ill patients)	8 (4)	7 (4)	
No data	5 (3)	3 (2)	
CGI-I score 1 wk after treatment			0.040
1 (Very much improved)	73 (41)	55 (31)	
2 (Much improved)	83 (46)	79 (44)	
3 (Minimally improved)	17 (9)	36 (20)	
4 (No change)	6 (3)	9 (5)	
5 (Minimally worse)	0 (0)	0 (0)	
6 (Much worse)	1 (0.6)	1 (0.6)	
7 (Very much worse)	0 (0)	0 (0)	
Time between partum and ECT			
0–4 wk	53 (29)	0 (0)	
4–6 wk	21 (12)	0 (0)	
6 wk to 3 mo	53 (29)	0 (0)	
3–6 mo	53 (29)	0 (0)	
Electrode placement			0.025
Unilateral	148 (82)	165 (91)	
Bitemporal	27 (15)	12 (7)	
Bifrontal	4(2)	2(1)	
No data	1 (0.6)	1 (0.6)	
Drug treatment within 100 d after ECT			
Antidepressants	122 (68)	133 (74)	0.202
Lithium	24 (13)	34 (19)	0.152
Antiepileptics	4(2)	10 (6)	0.102
Benzodiazepines	73 (41)	54 (30)	0.036
Antipsychotics	80 (44)	84 (47)	0.672
No. previous psychiatric admissions			0.004
0	59 (33)	45 (25)	
1	44 (24)	50 (28)	
2–3	42 (23)	29 (16)	
4–10	29 (16)	32 (18)	
≥11	6 (3)	24 (13)	

significant between-group differences were revealed by the univariate analysis. Statistical significance was defined as P < 0.05.

RESULTS

Comparison of Cases and Controls

Baseline characteristics of the 180 patients in the cases and 180 controls are summarized in Table 1. Of the 180 patients in each group, 83 had had psychosis, and 97 had depression without psychosis. The mean age was 30.5 (SD, 6.9) years among controls and 30.0 (SD, 5.4) years among cases. A significantly higher proportion of patients in the case group had a college education, and fewer patients in the case group were unemployed compared with the control group. Comorbidities were more common among controls. The MADRS-S was available among 94 of the controls and 93 of the cases treated for depression. The mean MADRS-S prior to ECT was 27.4 (SD, 13.4) among controls and 25.3 (SD, 13.8) among cases (P = 0.23). The CGI-I score 1 week after ECT was improved among most of the patients in both groups. However, the case group had more patients with lower scores (greater improvement after ECT) than did the control group. The majority of the patients in both groups had unilateral electrode placement, but the proportion was higher in the control group. Compared with the control group, a significantly higher proportion of patients in the case group had not had any previous admissions, and a lower proportion had had 11 or more previous hospitalizations. More cases than controls received benzodiazepines after ECT.

Relapse (Rehospitalization or Suicide)

The mean duration of the time to relapse or end of the follow-up period was 440 (SD, 475) days for the control group and 621 (SD,

548) days for the case group. In the control group, 102 patients (57%) relapsed; 101 of these were rehospitalized, and 1 committed suicide. In the case group, 73 patients (41%) relapsed, and none committed suicide. Thus, 78 patients (43%) in the control group, and 107 patients (59%) in the case group did not relapse.

The risk of relapse is depicted by a Kaplan-Meier curve in Figure 1. The risk of relapse was lower for the cases than the controls (P = 0.001). The risk of relapse after 6 months, calculated using the Kaplan-Meier estimator, was 28% for the cases and 39% for the controls. After 1 and 2 years, the risk of relapse was 31% and 40% for the cases, and 50% and 55% for the controls, respectively.

Factors Associated With Relapse

Table 2 shows the univariate associations of relapse. The cases had a lower risk of relapse than did the controls. Less improvement after ECT was most significantly associated with relapse. Many previous psychiatric admissions were also strongly associated with relapse. Other factors that were associated with relapse were unemployment, an education level less than high school, comorbid personality disorder, anxiety disorder, and substance use disorder, as well as treatment with antiepileptics and benzodiazepines within 100 days after ECT. There was no significant difference in relapse risk between controls with children and controls without children.

Table 3 shows the multivariate model. In this model, cases tended to have a lower risk of relapse than the controls (P = 0.051). Treatment with benzodiazepines, previous admissions (4–10 and ≥11), and less improvement after ECT were also associated with an increased risk of relapse.

DISCUSSION

To our knowledge, this is the first study that compares the relapse rates after ECT for women with PPD and/or psychosis with relapse rates after ECT for women outside this period. The Q-ECT provided a large number of patients who had received ECT in the postpartum period; furthermore, by linkage to several other registries, it was possible to closely match the cases and the controls. We found a lower risk of relapse after ECT for patients with PPD and PPP than for patients who received ECT outside the postpartum period.

The time period around childbirth is a risk factor for relapse in psychiatric disorders¹⁵ and probably contributed to the symptoms that led to ECT in the postpartum group. Months after childbirth, this risk diminishes. Although the risk of relapse was decreased in the postpartum group, it was substantial in both groups.

Most of the patients who relapsed did so within the first 6 months after ECT (27% in the postpartum group and 39% in the nonpostpartum group). This time frame is in line with that in previous studies of relapse after ECT (not postpartum).30,31 The 37% to 41% relapses in previous studies are also similar to the proportions in the present study. However, definitions of relapse in studies differ. In this study, we only considered rehospitalizations and suicide. In other studies, symptomatic worsening that does not require hospitalization has also been included. Should we have had the opportunity to include such symptomatic worsening, the relapse rates would have been higher. The high relapse rates seen in this and other studies reflect the fact that patients who receive ECT are often severely ill and difficult to treat.

Before ECT, most of the patients had high CGI-S scores of 5 (markedly ill) or 6 (severely ill). Severity of depression is reported to be a predictor for relapse. 14 However, in this study, the severity of the symptoms before ECT was not significantly associated with relapse. Possibly, patients who received ECT with less severe symptoms tended to have had pharmacotherapy for longer periods of time without sufficient benefit. If so, these patients probably had less benefit from prophylactic pharmacotherapy than did patients with more severe symptoms prior to ECT, which may offset the association between severity of symptoms and relapse risk.

Improvement after ECT was associated with a decreased risk of relapse in the univariate model, and a trend remained in the

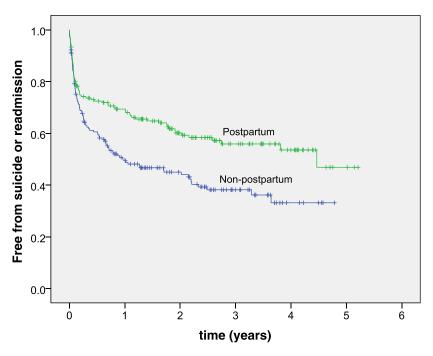


FIGURE 1. Proportion free from rehospitalization or suicide after ECT for PPD or psychosis compared with matched controls treated outside the postpartum period.

TABLE 2. Results of Univariate Cox Regression Analysis on the Risk for Relapse (Rehospitalization or Suicide) After ECT Postpartum and Nonpostpartum

	HR (95% CI)	P
Postpartum cases (reference: controls)	0.61 (0.45-0.83)	0.001
Age at treatment start, y		
16–25	1.12 (0.71–1.78)	0.625
26–30	1.29 (0.86-1.95)	0.226
31–35	1.10 (0.69-1.75)	0.689
36–45	Reference	
Marital status		
Married/cohabiting	0.958 (0.62-1.47)	0.845
Divorced	1.04 (0.59-1.84)	0.884
Unmarried	Reference	
Living with someone	1.34 (0.98-1.84)	0.067
Children		
Cases	0.676 (0.479-0.953)	0.025
Controls with children	1.297 (0.875–1.923)	0.195
Controls without children	Reference	
Education level		
Less than high school	1.66 (1.14–2.41)	0.008
High school	1.20 (0.85–1.71)	0.287
College	Reference	
Unemployed	1.85 (1.35–2.53)	0.000
Psychosis	0.94 (0.70–1.27)	0.677
Comorbidities	(() ()	
Personality disorder	2.47 (1.52-4.00)	0.000
Substance use disorder	2.24 (1.54–3.26)	0.000
Anxiety disorder	2.20 (1.56–3.08)	0.000
Attention-deficit/hyperactivity disorder	1.74 (0.94–3.04)	0.060
Severity of the disease before ECT acc	ording to the CGI-S sco	ore
4 (Moderately ill)	Reference	
5 (Markedly ill)	1.03 (0.63-1.69)	0.894
6 (Severely ill)	0.98 (0.60–1.61)	0.938
7 (Among the most extremely ill patients)	0.58 (0.22–1.54)	0.274
CGI-I score 1 wk after treatment		
1 (Very much improved)	Reference	
2 (Much improved)	1.21 (0.85–1.72)	0.301
3 (Minimally improved)	2.10 (1.36-3.25)	0.001
4 (No change)	2.13 (1.08-4.19)	0.030
6 (Much worse)	21.42 (5.04-91.07)	0.000
Electrode placement		
Unilateral	Reference	
Bitemporal	0.90 (0.55-1.47)	0.674
Bifrontal	0.50 (0.12-2.00)	0.324
Drug treatment 100 d after ECT		
Antidepressants	0.99 (0.71-1.38)	0.992
Lithium	1.08 (0.72–1.60)	0.718
Antiepileptics	2.02 (1.07–3.84)	0.031
Benzodiazepines	1.52 (1.13–2.05)	0.006
Antipsychotics	1.19 (0.88–1.60)	0.253

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TABLE 2. (Continued)

No. previous psychiatric adr	missions	
0	Reference	
1	0.98 (0.62–1.53)	0.916
2–3	1.35 (0.86–2.12)	0.195
4–10	2.10 (1.35–3.27)	0.001
≥11	3.38 (2.06–5.54)	0.000

CI indicates confidence interval; HR, hazard ratio.

multivariate model. The 2 patients with increased symptoms after ECT relapsed. This was not a surprising result, as these patients had symptoms that were not successfully treated by ECT or previously by pharmacotherapy. Only these 2 patients had symptomatic worsening after ECT, whereas most patients experienced a good initial effect from the ECT.

We also found that a higher number of previous admissions were associated with a higher risk of relapse. This supports findings from several previous studies that found that the number of previous admissions and episodes is strongly associated with relapse in depression. ^{14,31–33} Previous personality disorder, anxiety disorder, and substance use disorder were associated with relapse in univariate models, but not in the multivariate model, where the number of previous hospitalizations was controlled for.

TABLE 3. Results of Multivariate Cox Regression Analysis on the Risk for Relapse (Rehospitalization or Suicide) After ECT for Depression or Psychosis Postpartum and Matched Controls Treated Outside the Postpartum Period

	HR (95% CI)	P
Postpartum cases (reference: controls)	0.72 (0.52–1.00)	0.051
Education level		
Less than high school	1.36 (0.85-2.19)	0.068
High school	1.36 (0.94-1.96)	0.106
College	Reference	
Unemployed	1.27 (0.86-1.89)	0.236
Comorbidities		
Personality disorders	0.91 (0.49-1.68)	0.764
Substance use disorders	1.01 (0.60-1.71)	0.978
Anxiety disorders	0.79 (0.51-1.22)	0.283
CGI-I score 1 wk after treatment		
1 (Very much improved)	Reference	
2 (Much improved)	0.99 (0.69-1.42)	0.949
3 (Minimally improved)	1.45 (0.91-2.32)	0.122
4 (No change)	1.60 (0.75-3.41)	0.224
6 (Much worse)	71.7 (10.32–498.30)	0.000
Drug treatment 100 d after ECT		
Antiepileptics	1.17 (0.59-2.29)	0.656
Benzodiazepines	1.46 (1.05-2.02)	0.024
No. previous psychiatric admissions		
0	Reference	
1	1.00 (0.63-1.59)	1.00
2–3	1.32 (0.83-2.11)	0.240
4–10	1.70 (1.03-2.82)	0.040
≥11	1.75 (0.84–3.62)	0.135

CI indicates confidence interval; HR, hazard ratio.

Treatment with benzodiazepines within 100 days after ECT was associated with an increased risk of relapse, in both the univariate and the multivariate models. Our findings support those of a previous study, where benzodiazepines were associated with an increased risk of relapse in bipolar depression after ECT.³¹ Indications bias could have contributed to the result. Patients with anxiety or insomnia may have been treated with benzodiazepines, and the underlying disease, rather than the treatment, might be the true cause for the association. Nevertheless, a high proportion of patients were treated with benzodiazepines within 100 days after ECT (41% in the case group and 30% in the control group). Benzodiazepines should be prescribed with prudence.

We found no significant association between relapse risk and low age, which conflicts with the findings of previous studies.¹⁴ However, all women in the study were of a similar age, thus limiting the power to detect differences.

Limitations

There are some limitations in this study. First, relapse was defined as rehospitalization or suicide. Thus, patients who had symptoms that were not severe enough to warrant rehospitalization may have been overlooked. Second, in previous studies, mothers with mental disorders have previously been observed to be readmitted less often compared with women with mental disorders who do not have children. 15 If this association arises because women with children are reluctant to be separated from their children and accept inpatient treatment despite severe symptoms, it could bias the result. However, we did not see an association between having children and lower relapse risk in the present study. Third, we only had access to data concerning time for ECT, and not when the symptoms began. Some patients' symptoms may have started before the postpartum period, in which case these patients would have been falsely placed in the case group. Indeed, patients who first experienced symptoms during the postpartum period but were treated with ECT later than 6 months after childbirth were excluded from the study or could even have been placed in the nonpostpartum control group. Fourth, it was not always possible to find controls who perfectly matched the age of the case. For instance, the oldest case was 42 years, and the oldest control was 45 years. Fifth, several possible predictors for relapse were not studied, such as vulnerability characteristics (childhood abuse, negative life events, and parental psychopathology); such factors have been identified as risk factors for relapse in patients with depression. 14 While it was not possible to obtain this information from the various registers in the present study, future studies may wish to consider investigating these factors more fully. Future studies should also compare the relapse rates of patients treated by ECT and patients treated by other therapies.

CONCLUSIONS

The risk of rehospitalization or suicide after ECT was lower for women who had been treated for PPD and/or PPP than for women who had been treated for depression and/or psychosis outside the postpartum period. This study thus offers some support to treatment with ECT in severe forms of PPD and/or PPP. Nevertheless, the risk of relapse is substantial in both groups. Treatment with benzodiazepines, a higher number of previous psychiatric admissions, and absence of improvement after ECT were associated with relapse. A closer follow-up or a more intense prophylaxis should therefore be considered for such patients.

ACKNOWLEDGMENT

The authros thank the patients, nurses, and doctors who provided data to the Swedish National Quality Register for ECT.

REFERENCES

- 1. Stewart DE, Vigod S. Postpartum depression. N Engl J Med. 2016;375: 2177-2186.
- 2. O'Hara MW, Schlechte JA, Lewis DA, et al. Prospective study of postpartum blues. Biologic and psychosocial factors. Arch Gen Psychiatry. 1991;48:801-806.
- 3. Bergink V, Rasgon N, Wisner KL. Postpartum psychosis: madness, mania, and melancholia in motherhood. Am J Psychiatry. 2016;173:1179-1188.
- 4. World Health Organization. ICD-10 Version: 2016 [Web site]. Available at: http://apps.who.int/classifications/icd10/browse/2016/en#/F50-F59. Accessed May 10, 2018.
- 5. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorder (DSM-5). Arlington, VA: American Psychiatric Publishing; 2013.
- 6. Davé S, Petersen I, Sherr L, et al. Incidence of maternal and paternal depression in primary care: a cohort study using a primary care database. Arch Pediatr Adolesc Med. 2010;164:1038-1044.
- 7. Hendrick V. Treatment of postnatal depression. BMJ. 2003;32:1003-1004.
- 8. O'Hara MW, McCabe JE. Postpartum depression: current status and future directions. Annu Rev Clin Psychol. 2013;9:379-407.
- 9. Grace SL, Evindar A, Stewart DE. The effect of postpartum depression on child cognitive development and behavior: a review and critical analysis of the literature. Arch Womens Ment Health. 2003;6:263-274.
- 10. Stewart RC. Maternal depression and infant growth: a review of recent evidence. Matern Child Nutr. 2007;3:94-107.
- 11. Rahman A, Iqbal Z, Bunn J, et al. Impact of maternal depression on infant nutritional status and illness: a cohort study. Arch Gen Psychiatry. 2004;61: 946-952.
- 12. Grunewald C, Nillsson M, Cnattingius S, et al. Mödradödligheten underskattad i Sverige. Registerstudie av död i samband med graviditet, förlossning och post partum. Lakartidningen. 2008;105:2250-2253.
- 13. Nager A, Szulkin R, Johansson S-E, et al. High lifelong relapse rate of psychiatric disorders among women with postpartum psychosis. Nord J Psychiatry. 2013;67:53-58.
- 14. Ten Have M, de Graaf R, van Dorsselaer S, et al. Recurrence and chronicity of major depressive disorder and their risk indicators in a population cohort. Acta Psychiatr Scand. 2018;137:503-515.
- 15. Munk-Olsen T, Laursen TM, Mendelson T, et al. Risks and predictors of readmission for a mental disorder during the postpartum period. Arch Gen Psychiatry. 2009;66:189-195.
- 16. Williams J. Best practice guidelines for mental health disorders in the perinatal period. BC Reproductive Mental Health Program, Perinatal Services BC. 2014.
- 17. Focht A, Kellner CH. Electroconvulsive therapy (ECT) in the treatment of postpartum psychosis. J ECT. 2012;28:31-33.
- 18. Rundgren S, Brus O, Båve U, et al. Improvement of postpartum depression and psychosis after electroconvulsive therapy: a population-based study with a matched comparison group. J Affect Disord. 2018;235:258-264.
- 19. Semkovska M, McLoughlin DM. Objective cognitive performance associated with electroconvulsive therapy for depression: a systematic review and meta-analysis. Biol Psychiatry. 2010;68:568-577.
- 20. Slade EP, Jahn DR, Regenold WT, et al. Association of electroconvulsive therapy with psychiatric readmissions in US hospitals. JAMA Psychiat. 2017:74:798-804
- 21. Uchida T, Kishimoto T, Koreki A, et al. Predictors of readmission after successful electroconvulsive therapy for depression: a chart review study. Int J Psychiatry Clin Pract. 2016;20:260-264.
- 22. Kessler U. Commentary on "Improvement of postpartum depression and psychosis after electroconvulsive therapy—a population-based study with a matched comparison group." J Affect Disord. 2018;238:351-352.

- 23. Elvin T, Nordenskjöld A. Kvalitetsregister ECT. Årsrapport 2016. Örebro, Sweden: Kvalitetsregister ECT; 2017.
- 24. Svanborg P, Asberg M. A comparison between the Beck Depression Inventory (BDI) and the self-rating version of the Montgomery Asberg Depression Rating Scale (MADRS). J Affect Disord. 2001;64:203-216.
- 25. Guy W. ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: National Institute of Mental Health; 1976.
- 26. Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. BMC Public Health. 2011;11:450.
- 27. Wettermark B, Hammar N, Fored M, et al. The new Swedish Prescribed Drug Register—opportunities for pharmacoepidemiological research and experience from the first six months. Pharmacoepidemiol Drug Saf. 2007; 16:726-735.
- 28. Socialstyrelsen. Dödsorsaksregistret [Web site]. Available at: https://www. socialstyrelsen.se/register/dodsorsaksregistret. Accessed April 11, 2018.

- 29. SCB. Longitudinell integrationsdatabas för sjukförsäkrings- och arbetsmarknadsstudier (LISA) 1990-2013. Bakgrundsfakta; Statistics Sweden: 2016.
- 30. Jelovac A, Kolshus E, McLoughlin DM. Relapse following successful electroconvulsive therapy for major depression: a meta-analysis. Neuropsychopharmacology. 2013;38:2467-2474.
- 31. Popiolek K, Brus O, Elvin T, et al. Rehospitalization and suicide following electroconvulsive therapy for bipolar depression—a population-based register study. J Affect Disord. 2018;226:146-154.
- 32. Hardeveld F, Spijker J, De Graaf R, et al. Recurrence of major depressive disorder across different treatment settings: results from the NESDA study. J Affect Disord. 2013;147:225-231.
- 33. Mueller TI, Leon AC, Keller MB, et al. Recurrence after recovery from major depressive disorder during 15 years of observational follow-up. Am JPsychiatry. 1999;156:1000-1006.