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Safety of and response to electroconvulsive therapy during pregnancy: Results from population-based nationwide registries

Tor Arnison[1] | Olof Rask[2] | Axel Nordenskjöld[3] | Pouya Movahed Rad[4]

[1]Clinical Epidemiology and Biostatistics, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

[2]Department of Clinical Sciences Lund, Division of Child and Adolescent Psychiatry, Lund University, Lund, Sweden

[3]University Health Care Research Center, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

[4]Department of Clinical Sciences, Division of Adult Psychiatry, Faculty of Medicine, Lund University, Lund, Sweden

Correspondence
Pouya Movahed Rad, Psychiatric Clinic in Lund, Lund's University Hospital Baravägen 1, 221 85 Lund, Sweden.
Email: pouya.movahed_rad@med.lu.se

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Abstract

Introduction: Psychiatric disorders are common during pregnancy, affecting up to 16% of pregnant women. Severe depression and anxiety have significant negative effects on the health of both the mother and the developing fetus. Electroconvulsive therapy (ECT) is considered a treatment option for pregnant women with severe psychiatric disorders when other treatments have been ineffective or pose risks to the fetus. Knowledge of the safety and efficacy of ECT during pregnancy, however, remains limited.

Methods: Data were obtained from nationwide registries of pregnant women in Sweden who received ECT for a severe psychiatric disorder from January 2008 to December 2021. ECT-related outcomes in pregnant women were compared by propensity score matching with a group of non-pregnant women who also received ECT. Pregnancy-related outcomes were compared with two additional control groups: one consisting of the same group of women who did not receive ECT during another pregnancy and the other composed of pregnant women admitted to inpatient psychiatric care but who did not receive ECT, matched based on propensity score.

Results: Ninety-five pregnant women received ECT during the study period, accounting for 97 pregnancies. The response rate to ECT in pregnant women ($n = 54$) was similar to the matched control group of non-pregnant women (74% vs. 65%; OR 1.61; 95% CI 0.79–3.27). Rates of adverse events related to ECT were similar to those in the control group. There were no pre-term births or severe adverse outcomes related to the pregnancy, that were close in time to ECT. Therefore, no adverse outcomes related to pregnancy and childbirth could be directly attributed to ECT. The likelihood of premature birth and a 5-min Apgar score <7 in the newborn were both significantly higher in the ECT group, compared with the matched non-ECT group (OR 2.33, 95% CI 1.15–4.73, $p = 0.008$, and OR 3.68, 95% CI 1.58–8.55, $p < 0.001$, respectively). By contrast, no significant differences were observed when women in the

pregnant ECT group were compared with the same group lacking ECT during another pregnancy.

Conclusions: ECT was associated with a positive treatment response in pregnant women with severe psychiatric disorders. The response rate to ECT was similar in pregnant and non-pregnant women. Nevertheless, the risks of premature birth and of a slightly poorer condition in newborns were higher in women who did than did not receive ECT, emphasizing the need for increased attention to severe psychiatric disorders during pregnancy.

KEYWORDS

electroconvulsive therapy, fetus, newborn, pregnancy, women

1 | INTRODUCTION

Psychiatric disorders, such as severe depression and anxiety, are highly prevalent during pregnancy, affecting up to 16% of women during pregnancy.[1,2] These disorders can have significant adverse effects on both the mother and the developing fetus.[3] Electroconvulsive therapy (ECT) is considered an option for pregnant women with severe psychiatric disorders when other treatments are ineffective or carry potential risks to the fetus. ECT provides a relatively rapid relief of symptoms, an advantage over other treatments, which may require a time lag of weeks to months to become effective.[4] ECT has shown promise as an effective treatment for severe psychiatric disorders, including major depressive disorder, during pregnancy.[5–8]

ECT involves the application of electrical current through the brain, inducing a seizure. ECT has been used since the 1930s to treat a variety of mental disorders, including major depressive disorder, manic disorder, and schizophrenia.[9]

Despite its potential benefits, ECT may carry potential risks for both the mother and the fetus. The primary concerns are risks such as miscarriage, preterm labor, and other obstetric complications. The use of anesthesia during ECT may also pose risks to the fetus, including hypoxia due to respiratory depression.[10–13]

Little is known about the safety and efficacy of ECT during pregnancy. Most studies have been case reports, small case series and retrospective studies with relatively few patients.[12,13] In addition, the content of these studies may have bias toward reporting safe use or adverse outcomes, making certainty of the evidence low. Additional research is needed to determine the risks and benefits of ECT in pregnant women more accurately.

Swedish national registries cover all inhabitants of the country and prospectively collect data to facilitate epidemiological surveillance and research. Such registries provide unique opportunities to study the outcomes of ECT in pregnant women.

Significant outcomes

- Ninety-five women who received electroconvulsive therapy (ECT) during 97 pregnancies were identified in Swedish nationwide registers between 2008 and 2021.
- The response rates after ECT were high in the pregnant women (74%), which were similar to those found in matched non-pregnant controls (65%).
- No adverse outcomes related to pregnancy and childbirth could be directly linked to ECT.

Limitations

- National register data, although vast in scope and coverage, is dependent on reporting. A limitation with the current study is therefore known, and potential unknown, missing data.
- The current study did not control for some factors that are associated with poor outcomes in pregnancy and birth, such as smoking, alcohol consumption, and obesity.
- ECT is often considered for the most severely ill patients and it is therefore challenging to identify matched controls of patients with similar illness severity, but who have not received ECT.

2 | AIMS OF THE STUDY

The primary aim of this study was to explore the indications, prevalence, response rate, and adverse events associated with ECT in pregnant women hospitalized for psychiatric disorders, and compare these with a propensity score matched control of non-pregnant

women who received ECT. Additionally, this study sought to assess the childbirth outcomes and well-being of newborns in these women and compare them with controls of pregnancies where the mother did not receive ECT.

3 | METHOD

3.1 | Participants and study design

The current study used data from Swedish nationwide registries, to assess response rates and risks of ECT during pregnancy. Information about pregnancies was obtained from the Swedish Medical Birth Registry (MBR), and information about ECT treatment was obtained from the National Quality Registry for ECT (Q-ECT) and the Swedish National Patient Registry (NPR). The study sample included all women in Sweden registered in either the Q-ECT or the NPR who received ECT while pregnant from January 2008 to December 2021. If more than one ECT treatment was registered per pregnancy, only the earliest by date was included. This group is henceforth labeled the "Pregnant ECT"—group. To facilitate comparison of response rates, only women with a non-missing value on the Clinical Global Impression-Improvement (CGI-I) scale were included in the response analysis. This sub-group is henceforth referred to as the "Pregnant ECT w. CGI-I" group. Response rates to ECT during pregnancy were compared with response rates in a control group of non-pregnant women who received ECT for a matched severe psychiatric disorder, referred to as the "Non-pregnant ECT" group.

To assess adverse events for mother and child associated with receiving ECT during pregnancy, two control groups were identified: One subgroup consisting of the same group of women who did not receive ECT during other pregnancies (henceforth called, the "Non-ECT additional pregnancy"—group) and the other consisting of women with a severe psychiatric disorder while pregnant who did not receive ECT during pregnancy (henceforth called the "Non-ECT pregnant inpatient"—group). In total, three subgroup comparisons were conducted in the study: (1) The "Pregnant ECT w. CGI-I" group was compared with the "Non-pregnant ECT" group, 2) The "Pregnant ECT" group was compared with the "Non-ECT pregnant inpatient" group, and (3) those in the "Pregnant ECT" group with additional pregnancies, with the "Non-ECT additional pregnancy" group. The subgroups, control groups and comparisons included in the study are depicted in Figure 1.

3.2 | Data sources and measures

The NPR is a mandatory registry that covers over 99% of inpatients. This registry includes admission and discharge dates, International Classification of Diseases (ICD) codes, treatment procedure codes, and patient demographic information.[14] The dataset evaluated in this study included 18,692,712 inpatient admissions. The present study recorded dates of admission and discharge for ECT (ICD codes DA006, DA024, DA025, and V9218), childbirth (ICD codes O00*, O01*, O03*, O04*, O05*, O06*, O80*, O81*, O82*, O83*, and O84*), and inpatient visits for affective psychiatric disorders without ECT (ICD codes: F31*, F32*, F33*, F530*, F20*, F23*, F25*, F06*, G20*, and G21*), as well as information on age during pregnancy and on comorbid psychiatric disorders.

The Q-ECT is a national quality registry, established in 2008 and instituted nationwide in 2012. The coverage has increased from 79% in 2012 to 96% in 2021,[14] and provides data on aspects related to ECT in Sweden. Between January 2008 and December 2021, this registry included 49,942 treatment series of ECT. Variables derived from the Q-ECT include dates of admission and discharge for ECT, indications for treatment, age at treatment, number of treatment sessions in a series, previous suicide attempts, involuntary/voluntary status, electrode placement, and anesthetic agents used. The baseline severity of psychiatric symptoms was assessed using the Clinical Global Impression-Severity (CGI-S) scale[15,16] and the self-reported version of the Montgomery-Åsberg Depression Rating Scale (MADRS-S).[17] Response to ECT within 1 week after finishing the index-ECT series was assessed using the Clinical Global Impression-Improvement (CGI-I) scale. Patients with CGI-I scores of 1 (very much improved) and 2 (improved) were regarded as responding to treatment.[16]

The MBR is a nationwide registry containing information on all pregnancies that have led to births since 1973.[18] The dataset evaluated in this study included 1,414,322 pregnancies. Variables recorded included parity, length of pregnancy in days, type of delivery (spontaneous or induced vaginal, vacuum extraction, or planned or acute Cesarean section), sex of the child, preeclampsia, diabetes, complications in mother and child, malformation at birth, stillbirth, Apgar scores at 1, 5, and 10-min after birth, child length and weight at birth, and the proportion of children large and small for gestational age.

Additional information about medication usage and ECT during pregnancy was obtained from the Swedish National Prescribed Drug Registry (PDR),[19] and demographic information about the patients (income, education level, cohabitation) was retrieved from the

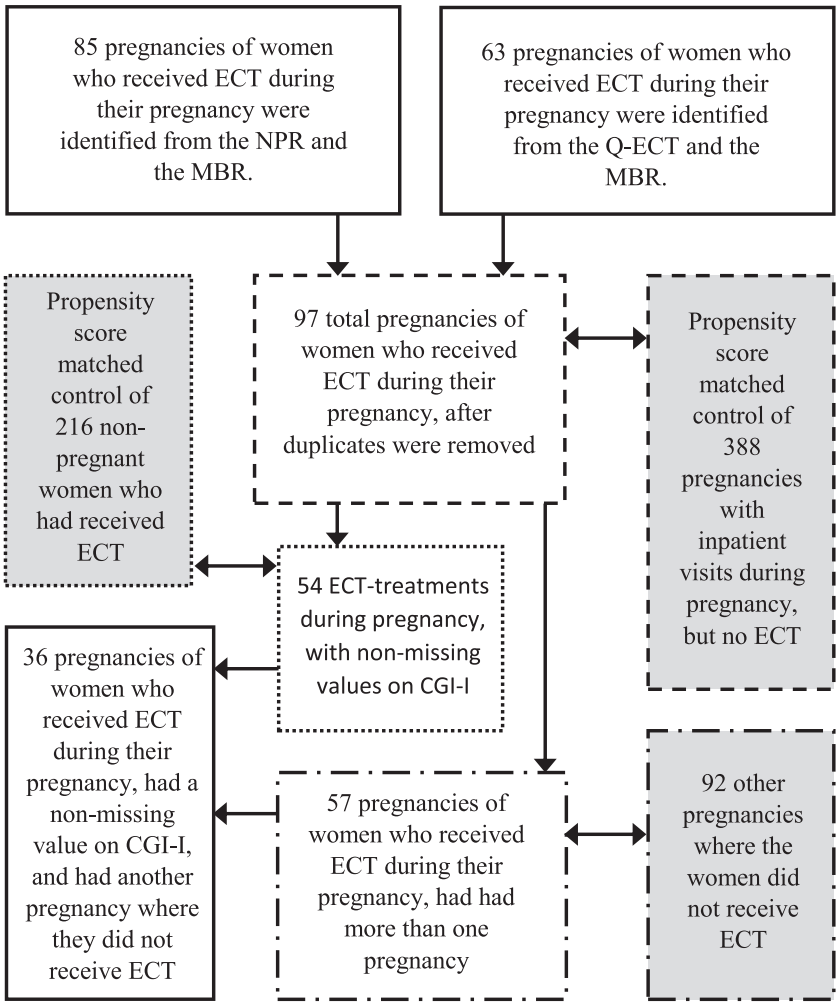

FIGURE 1 Flowchart depicting the inclusion process of the case group and the control groups in the current study. The control groups are indicated by gray shading. The three comparisons are indicated by the line around the boxes: dotted lines, dashed lines, and mixed dotted and dashed lines. MBR, The Swedish Medical Birth Register; NPR, The Swedish National Patient Register; Q-ECT, The Quality Register for ECT.

Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA).[18]

3.3 | Statistical analyses

All data handling and statistical analyses were performed using SAS v. 9.4. The control groups were propensity score matched with the case group at a 1:4 ratio, using an optimal matching algorithm with maximum 0.2 caliper width in propensity score logit.[20] Control group 1, henceforth labeled the "Non-pregnant ECT"—group, was propensity score matched on age, CGI-S at baseline, psychopharmacological treatments during ECT, and comorbid anxiety- and personality-disorders, as well as exactly matched on sex, indication for treatment, and use of lithium and antiepileptic agents. The purpose of this matching procedure was to minimize differences in illness severity and concurrent treatments at baseline. Control group 2, consisting of pregnant women who did not receive ECT (the "Non-ECT pregnant inpatient"—group) was propensity score matched on age, parity, concurrent psychopharmacological treatments, comorbid anxiety disorders, as well as exactly matched on preeclampsia and diabetes. The purpose of this matching procedure was to minimize differences in factors that might contribute to adverse outcomes during pregnancy and childbirth. Balance between groups in matching variables was assessed by calculating standardized mean differences (SMD), with a cutoff <0.1,[21] and are displayed in Tables 2 and 3.

Differences between groups in the main outcomes (CGI-I after ECT, proportion of premature births and proportion of infants with 5-min Apgar scores <7) were assessed by calculating odds ratios (ORs) and 95% confidence intervals (CIs),[22] with significance tests by conditional binomial logistic regression analyses. In a logistic regression analysis, the logistic function is utilized to estimate the probability of a binary outcome given specific values on one or several predictors. A conditional logistic regression is an extension of logistic regression that is suitable for observational case–control studies since it accounts for matching by having a unique constant term for each stratum.[23,24]

Because sample coverage across the different group comparisons was incomplete, sensitivity analysis was performed (see Data S1) comparing the "Pregnant ECT"—group with two additional sub-groups of this sample: One sub-group which included those with more than one pregnancy, and one sub-group of women who had a non-missing value on CGI-I and had at least one additional pregnancy registered where they had not received ECT.

4 | RESULTS

4.1 | Patient characteristics

A total of 95 pregnant women in Sweden received ECT during a total of 97 pregnancies within the period from January 2008 to January 2021 (Table 1).

4.2 | Rates of response to ECT during pregnancy

The Q-ECT included 54 patients who received 416 sessions of ECT during pregnancy and had non-missing values on the CGI-I scale. These 54 ECT series were propensity score matched with 216 non-pregnant women registered in the Q-ECT who had received ECT (Table 2).

TABLE 1 Demographic characteristics of the 95 women who received electroconvulsive therapy during pregnancy.

No. of pregnant women	95
Mean age, year (SD)	31 (6)
Occupation	
Employed	69
Self-employed	2
Not recorded	24
Education level, highest attained	
Elementary school, year	18
Secondary school, year	38
Higher education, <3 years	22
Higher education, ≥3 years	14
Not recorded	3
Marital status	
Unmarried	72
Married	16
Divorced	6
Not recorded	1

Response rates after ECT were similar in pregnant women and a matched control group of non-pregnant women (OR 1.61; 95% CI 0.79–3.27, p 0.19). Rates of adverse events were lower in the "Pregnant ECT w. CGI-I" group than in the "Non-pregnant ECT" group (17% vs. 30%), although the difference was not statistically significant (OR 0.63, 95% CI 0.29–1.38, p 0.25). Changes in fetal heart rate as adverse events were reported in three (5%) pregnant women.

4.3 | Pregnancy-related safety of ECT during pregnancy

ECT was administered during 97 pregnancies. This group was compared with two control groups: the "Non-ECT pregnant inpatient"—group, consisting of 388 propensity score matched controls, and the "Non-ECT additional pregnancy"—group; the latter consisted of 55 women in the ECT-group with more than one pregnancy during 92 pregnancies when they did not undergo ECT (Table 3). The groups are compared on maternal characteristics in Table 3, and on pregnancy- and child-outcomes in Table 4, below.

Overall, the rates of reported adverse events related to childbirth, as well as adverse outcomes in the child, were similar in the "Pregnant ECT"—group compared with the control groups. The fetal malformations, which were also comparable across the groups, included cardiac septal defects, accessory finger or auricle, congenital cataract, Chiari malformation, hypospadias, undescended testicle, unstable or dislocated hip, pulmonary artery stenosis, and achondroplasia. Comparisons of the "Pregnant ECT"—group with the "Non-ECT pregnant inpatient"—group showed that the proportion of vaginal births was similar (66% vs. 61%, OR 1.28, 95% CI 0.77–2.13, $p = 0.34$), but that the former had a significantly higher rate of induced deliveries (34% vs. 20%, OR 2.30, 95% CI 1.35–3.93, $p < 0.01$), as well as a non-significant trend for Cesarean sections (31% vs. 23%, OR 1.44, 95% CI 0.84–2.48, $p = 0.19$). When compared with the "Non-ECT additional pregnancy"—group, pregnancies with ECT showed significantly higher rates of induction (34% vs. 20%, OR 2.67, 95% CI 1.11–6.45, $p = 0.03$) and tended toward higher rates of Cesarean sections (31% vs. 12%, OR 2.90, 95% CI 0.86–9.85, $p = 0.09$). The two most noticeable variables were premature deliveries, which appeared more prevalent in the "Pregnant ECT"—group than in the controls, as well as lower Apgar scores which indicated less healthy infants shortly after birth in the "Pregnant ECT"—group.

TABLE 2 Clinical characteristics of women who received electroconvulsive therapy (ECT) for a severe mental illness either during pregnancy or without being pregnant.

Variable		*n*	Pregnant ECT w. CGI-I—group	Non-pregnant ECT—group	SMD
Age, mean (SD), year		54	30 (6)	30 (7)	<0.01
Indications for ECT, *n* (%)		54			
	(2)F32.2 Major depressive disorder, single episode, severe without psychotic features. *n* (%)		13 (24)	52 (24)	0
	(3)F32.3, Major depressive disorder, single episode, severe with psychotic features. *n* (%)		8 (15)	32 (15)	0
	(1)F32.1, Major depressive disorder, single episode, moderate. *n* (%)		5 (9)	20 (9)	0
	(4,5,6)Major depressive disorder, recurrent. n (%)		11 (20)	44 (20)	0
	Bipolar disorder, without psychotic features. *n* (%)		9 (17)	36 (17)	0
	Bipolar disorder, with psychotic features. *n* (%)		3 (6)	12 (6)	0
	Primary psychotic symptoms, *n* (%)		5 (9)	20 (9)	0
Involuntary-voluntary status		39			
n (%)	Voluntary care		24 (62)	96 (62)	0
n (%)	Involuntary care		15 (39)	60 (39)	0
n (%)	Forensic psychiatry		0 (0)	0 (0)	0
Previous suicide attempts		15			0.42
n (%)	No		12 (80)	27 (49)	
n (%)	Yes		3 (20)	28 (51)	
Previously received ECT, proportion yes (%)		39	11 (28)	16 (11)	0.38
Number of sessions in treatment series, mean (SD)		63	6.6 (3)	7.5 (4)	2.22
Timing of ECT		37			
	Trimester 1 only		10 (27)	-	
	Trimester 1 + 2		3 (8)	-	
	Trimester 2 + 3		6 (16)	-	
	Trimester 3 only		18 (49)	-	
CGI-S pretreatment, mean (SD)		53	5.4 (1)	5.4 (1)	0
MADRS-S pretreatment, mean (SD)		20	34.9 (10)	33.7 (12)	−0.10
CGI-I post treatment mean (SD)		54	1.8 (1)	2.0 (1)	−0.04
Response rate (proportion 1 and 2 on CGI-I)		54			−0.15
	Yes, *n* (%)		40 (74)	141 (65)	
	No		14	75	
Electrode placement		54			
n (%)	Unilateral		42 (78)	195 (90)	0.30
n (%)	Bitemporal		12 (22)	16 (7)	−0.37
n (%)	Bifrontal		0 (0)	5 (2)	0.15

TABLE 2 (Continued)

Variable		n	Pregnant ECT w. CGI-I—group	Non-pregnant ECT—group	SMD
n (%)	Other		0 (0)	0 (0)	0
Anesthetic agents		39			
n (%)	Thiopental		21 (54)	102 (63)	0.14
n (%)	Propofol		15 (41)	54 (33)	−0.12
n (%)	Other		3 (8)	6 (4)	−0.03
Medication during ECT		20			
n (%)	Antidepressants		14 (70)	60 (72)	0.05
n (%)	Lithium		1 (5)	4 (5)	0
n (%)	Benzodiazepines		4 (20)	42 (51)	0.63
n (%)	Antipsychotics		6 (30)	50 (60)	0.51
n (%)	Antiepileptics		0 (0)	0 (0)	0
Reported adverse events		9			−0.10
	"Disturbed memory functioning"		4 (7)	28 (13)	
	"Headache"		0 (0)	22 (10)	
	"Complications related to fetal heart rate"		3 (6)	0 (0)	
	Other		2 (4)	14 (7)	

Note: SMD, standardized mean difference; *n*, sample size of the case group for each variable.

TABLE 3 Comparison on maternal characteristics of women who received ECT during pregnancy ($n = 97$), with (1) women who received inpatient care, but not ECT, for a psychiatric disorder during pregnancy, (2) and the same group of women who did not receive ECT during other pregnancies.

Maternal characteristics				
Variable	Pregnant ECT—group ($n = 97$)	Non-ECT pregnant inpatient—group ($n = 388$)	Non-ECT additional pregnancy—group ($n = 92$)	SMD
N				
Age, mean (SD)	31.0 (5.5)	30.8 (6)	27.9 (6)	0.03
Parity, *n* (%)				0.07
1	50 (52)	205 (53)	40 (44)	
2	27 (28)	111 (29)	28 (30)	
3	11 (11)	48 (12)	16 (17)	
4+	9 (9)	24 (6)	8 (9)	
Diabetes, *n* (%)	5 (5)	20 (5)	3 (3)	0
Preeclampsia, *n* (%)	3 (3)	12 (3)	3 (3)	0

Abbreviations: ECT, electroconvulsive therapy; SMD, standardized mean difference.

4.4 | ECT in relation to premature delivery, Apgar score, and stillbirth

Of the 97 pregnancies involving ECT, 14 resulted in premature deliveries. The median gestation length for premature birth was 35 weeks and 3 days (range 23 weeks and 0 days to 36 weeks and 5 days), and all but two premature births occurred after the 32nd week of gestation (Table 4). In only one of these 14 premature births, there was an induced delivery or an acute Cesarean section within days of ECT: an acute Cesarean section registered 3 days after the last ECT. The OR

TABLE 4 Comparison on birth- and child-outcomes of women who received electroconvulsive therapy (ECT) during pregnancy ($n = 97$), with (1) women who received inpatient care, but not ECT, for a psychiatric disorder during pregnancy, (2) and the same group of women who did not receive ECT during other pregnancies.

Variable		Pregnant ECT—group ($n = 97$)	Non-ECT pregnant inpatient—group ($n = 388$)	Non-ECT additional pregnancy—group ($n = 92$)
Length of pregnancy in days, mean (SD)		267 (22)	275 (13)	273 (16)
Delivery, *n* (%)				
Spontaneous		43 (44)	241 (62)	70 (76)
Induced		33 (34)	79 (20)	18 (20)
Cesarian		21 (22)	64 (17)	4 (4)
Not recorded		0	4	0
Planned Cesarean section		11 (11)	42 (11)	2 (2)
Acute Cesarean section		19 (20)	48 (12)	9 (10)
Vaginal birth		64 (66)	236 (61)	71 (77)
Forceps and/or vacuum extraction		3 (3)	34 (9)	6 (7)
Not recorded		0	28	4
Premature birth (<37 weeks), *n* (%)		14 (14)	35 (9)	10 (11)
34–37 weeks		8 (8)	26 (7)	7 (7)
32–34 weeks		5 (5)	4 (1)	2 (2)
30–32 weeks		0 (0)	3 (1)	1 (1)
<30 weeks		1 (1)	2 (1)	0 (0)
Apgar 5 min				
n (%)	0–3	0 (0)	0 (0)	0 (0)
n (%)	4–6	9 (9)	8 (2)	2 (2)
n (%)	7–10	86 (89)	370 (95)	89 (97)
Malformation (*n*, %)		3 (3)	15 (4)	4 (4)
Child weight at birth in grams, mean (SD)		3251 (738)	3421 (629)	3461 (700)
Birth size				
n (%)	Small for gestational age	3 (3)	22 (6)	1 (1)
n (%)	Appropriate for gestational age	85 (88)	355 (89)	86 (94)
n (%)	Large for gestational age	9 (9)	20 (5)	5 (5)
Stillbirth (%)		2 (2)	1 (<1)	1 (1)

for premature birth was significantly higher in the "Pregnant ECT"—group than in the "Non-ECT pregnant inpatient"—group (OR 2.33, 95% CI 1.15–4.73, $p = 0.002$), but not to the "Non-ECT additional pregnancy"—group (OR 2.16, 95% CI 0.75–6.22, $p = 0.156$). The OR for a 5-min Apgar score <7 was significantly higher in the "Pregnant ECT" group than in the "Non-ECT pregnant inpatient"—group (OR 3.68, 95% CI 1.58–8.55, $p < 0.001$), but not compared with the "Non-ECT additional pregnancy"—group (OR 2.53, 95% CI 0.59–10.90, $p = 0.21$).

Of the 14 premature births, four (29%) mothers continued ECT treatment after childbirth, with all four children delivered by Cesarean section, either planned or

acute. In two of these cases, ECT and childbirth were registered during the same inpatient visit, both involving delivery by planned Cesarean section. The remaining two children were delivered by acute Cesarean section, 3 and 31 days after the last ECT session, respectively. Most of the mothers with premature births had risk factors that may contribute to premature labor, including preeclampsia, hypertension, diabetes, Crohn's disease, and oligohydramnios. Out of these 14 infants, four (29%) had 1-min Apgar scores below 7, three (21%) had 5-min Apgar scores below 7, and three (21%) had 10-min Apgar scores below 7.

Two (2%) of the 97 pregnancies involving ECT ended in stillbirth, these mothers had received ECT 34 and 97 days before delivery, respectively.

5 | DISCUSSION

This nationwide registry study, with data collected over a span of 14 years, explored response rates to ECT and its potential side effects in pregnant women with severe psychiatric disorders. Analysis of 97 pregnancies registered in the Q-ECT and NPR found that ECT appeared safe with no severe adverse events directly linked to ECT. An analysis of 416 ECT sessions in 54 pregnant women demonstrated high response rates. These findings suggest that ECT should be considered a feasible treatment option for pregnant women with severe psychiatric illnesses.

ECT had a response rate of 74% in these pregnant women, similar to the response rate in non-pregnant women (65%) and in agreement with results obtained in studies of adults included in the Swedish ECT registry.[25] Depression was the most prevalent diagnosis among patients who underwent ECT, in agreement with findings from other studies involving psychiatric patients who underwent ECT.[26]

The reported adverse events of ECT in pregnant women included headache and transient memory impairment, consistent with previous findings.[27,28] Although the present study cannot rule out the possibility that other complications may be associated with ECT, such as aspiration pneumonia, sustained seizures, or allergic reactions to anesthetic agents, such types of adverse events were not reported in the data and have rarely been reported in previous studies.[29]

The dataset evaluated in this study included nearly all individuals who underwent ECT throughout Sweden. ECT was generally not associated with an increased risk of adverse pregnancy-related outcomes. However, ECT was associated with two specific outcomes, including a significant higher incidence of premature birth (around 12%) in both the case and control groups, surpassing the 5% rate reported by the Swedish National Board of Health and Welfare in the general population.[30] Furthermore, this risk was higher among pregnant women who underwent ECT for severe psychiatric disorders than among women with similar diagnosis who did not undergo ECT, but was similar to the risk in the same women who did not undergo ECT during other pregnancies. In addition, the risk of newborns having 5-min Apgar scores <7 was higher in women with severe psychiatric disorders who did than did not undergo ECT, but was not higher in the same women who did not undergo ECT during other pregnancies. Preterm birth, operative or instrumental delivery, and low socioeconomic status comprise some of the risk factors associated with a low Apgar score,[31,32] and may have caused the low Apgar scores observed in the current study. Taken together, these findings suggest that there is an impact of severe psychiatric disorders, illustrated by the need for ECT, on adverse events. However, weighing in the potential impact of other risk factors, such as smoking and obesity, previous research has indicated that the combined impact of these may cause the lion's share of adverse effects.[33–35]

In the present study, a comparison of women who received ECT during pregnancy with women with similar diagnoses who did not, showed that the proportions of induced deliveries and Cesarean sections were higher in the former. Similar results were observed when comparing these rates in women who received ECT during pregnancy with findings in the same women, when they did not undergo ECT during other pregnancies.

Although 14 women who received ECT during pregnancy gave birth prematurely, only four had ongoing ECT at the time of delivery. In three of these women, ECT and childbirth were registered during the same inpatient visit. Two of these had ECT and delivery registered on the same day, although both were delivered by planned Cesarean section: This indicates that, rather than ECT inducing delivery, both appeared to have been a priori planned to occur on the same day. We could not find any association of ECT with fetal malformation. Individual risk factors for prematurity, such as severe psychiatric illness and overweight, may be responsible for the association of ECT with premature birth. The high incidence of premature births in the control groups is in line with this hypothesis. Nonetheless, these high rates of premature births are highly concerning, given that premature birth is related to long-term negative health effects.[36] Even if ECT in itself may not be associated with premature birth, clinicians who administer ECT must be cognizant that they are working with a vulnerable patient population with heightened risk of pregnancy-related complications.[37]

Stillbirths were observed in two pregnant women who received ECT, compared with one stillbirth in the control group. These outcomes in the general population are rare, with prevalence rates of 0.3%–0.5%, suggesting that they may be associated with severe psychiatric disorders. Psychiatric disorders often involve risk factors, such as medication use, inadequate prenatal care, substance abuse, and social determinants of health, which can contribute to adverse pregnancy outcomes.[37,38] Because ECT is regarded as a treatment primarily in very severe cases, patients who underwent ECT may be more ill or experienced significantly longer pretreatment stress. Notably, the mothers of these two stillborn infants had received their last ECT 97 and 34 days, respectively, before delivery. The time lag makes a causal link between stillbirth and ECT unlikely. Regardless, it is important to underscore that the current data is not sufficiently detailed to rule out a potential link between stillbirth with ECT, and we hope that future research may bring more light to this crucial question.

Because of the potential confounding factors, small sample size, and complexities of the causal relationship between ECT and pregnancy outcomes, additional studies in larger populations and more comprehensive control groups are necessary to better understand the relationships between ECT and pregnancy outcomes. Such study-populations may be hard to come by, and may require international collaboration.

Abnormal fetal heart rates were observed during three pregnancies in women who underwent ECT, but none in the control group. This finding emphasizes the importance of closely monitoring fetal well-being throughout pregnancy. However, the findings observed in patients who received ECT may be due to enhanced surveillance of this group compared with pregnant women who did not undergo ECT.

To our knowledge, this study represents the largest population of pregnant women treated with ECT in a naturalistic setting. The data on diagnosis, treatment effects, and other ECT-related outcomes were prospectively collected in the Q-ECT. Nevertheless, because this was a registry study, all the data relied on reporting. In addition, this is the first study to our knowledge to compare pregnancy-related outcomes in hospitalized depressed pregnant women who did and did not undergo ECT. Despite propensity score matching based on relevant variables, additional confounders may be unaccounted for in the registry data, such as differences regarding alcohol, substance use, obesity, and smoking habits between the groups. Such factors have been shown to negatively impact pregnancy-related outcomes in previous research,[33–35] and may have confounded the results of the current study. We recommend future studies to account for such factors. In addition, pregnant women who received ECT may have had more severe illness than women who did not receive ECT. Conversely, other factors, including underlying medical conditions, may have influenced the decision to perform or not perform ECT. Another limiting factor was the incomplete coverage of data, with responses to treatment and pregnancy-related outcomes therefore being based on different, albeit highly overlapping, samples. This limited the ability to establish associations between treatment outcomes and adverse pregnancy-related events. Nonetheless, sensitivity analyses (Data S1) indicated that the differences between the patients included in the analyses of responses to treatment and pregnancy-related outcomes, after adjusting for potential confounders, were minor.

Different international clinical guidelines offer different perspectives on the use of ECT during pregnancy. While the APA guidelines[39] and the Australian and New Zealand guidelines[40] assert the general safety of ECT for both the mother and the fetus, the Australian guideline even suggests it as the preferred treatment option for severe mood disorders.[40] In contrast, the NICE Guideline takes a cautious stance due to limited evidence regarding its safety.[41] It recommends using ECT with caution and emphasizes the urgent need for further research to evaluate its effectiveness and safety in pregnant women. This study meaningfully contributes to bridging the existing knowledge gap by demonstrating a high response rate and a predominantly safe profile of ECT for both the mother and the fetus in patients with severe psychiatric disorders. When considering ECT in this patient population, it is essential to also consider the alternative to ECT, since the decision not to provide ECT could potentially result in more severe negative outcomes. Considerations include the patient's ability to manage her own health, and indirectly the health of the fetus, in absence of effective treatment. Further considerations include the fetal risks associated with psychopharmacologial alternatives, and the potential for ongoing psychiatric illness during pregnancy to increase the risk of more severe postpartum psychiatric illness, such as postpartum psychosis.

To Conclude, this study assessed safety and response to ECT in pregnant women. Between 2008 and 2021, ECT was delivered during 97 pregnancies for a total of 416 sessions. The most common indication for ECT was a current episode of Major Depression, followed by an episode related to Bipolar disorder. In 31% of the cases, the woman had psychotic symptoms at the time of ECT. The results showed high response rates in women who received ECT during pregnancy, with no adverse events that could be directly linked to ECT. This study adds an important piece of the puzzle to fill the existing

knowledge gap regarding safety and efficacy of ECT in pregnant women and may inform future clinical guidelines on this topic. Nevertheless, it is important to note that pregnant women who are offered ECT are often dealing with severe illness and an increased risk of adverse outcomes. When evaluating treatment options, a thorough assessment of potential risks becomes imperative. This includes considering the consequences of not performing a fast and effective treatment like ECT, the risks associated with untreated mental illness, and the limitations and potential risks of pharmacological interventions for both the mother and the child.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/acps.13623.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Axel Nordenskjöld upon reasonable request.

ETHICS STATEMENT

The study was approved by the Regional ethics vetting board of Uppsala (registration number 2014/174) and the Swedish Ethical Review Authority (2021-03815). Patients could choose not to have data on ECT included in the Swedish National Quality Registry.

ORCID

Tor Arnison https://orcid.org/0000-0002-9035-0287
Olof Rask https://orcid.org/0000-0003-0565-3812
Axel Nordenskjöld https://orcid.org/0000-0001-7454-3065
Pouya Movahed Rad https://orcid.org/0000-0003-2041-3550

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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