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Postpartum depression in women with epilepsy versus women without epilepsy

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Abstract

The goal of this study was to determine if there is a significant difference in the rate of postpartum depression among patients with epilepsy and healthy controls. All patients were recruited from the Epilepsy Center and the Department of Obstetrics and Gynecology, University of Milan, St. Paolo Hospital (Milan, Italy). Thirty-five pregnant women with epilepsy and an equal number of pregnant women without epilepsy were assessed with the Edinburgh Postnatal Depression Scale (EPDS), a clinical interview used to screen for postpartum depression (PPD), and a sociodemographic questionnaire. The rate of PPD in patients with epilepsy was statistically significantly higher than that of the controls ($P < 0.05$). PPD was present in 29% of the patients with epilepsy and 11% of the controls. In conclusion, it is very important to point out that in our pilot study, the rate of PPD was higher among women with epilepsy than among women without epilepsy. In this regard, women at higher PPD risk can be identified earlier and treated as soon as possible to alleviate their symptoms and improve their quality of life.

Keywords: Postpartum depression; Epilepsy; Pregnancy; Edinburgh Postnatal Depression Scale

1. Introduction

Childbirth for women is a time of great vulnerability, and postpartum mood disorders represent the most frequent form of maternal morbidity following delivery [1,2]. These affective disorders range in severity from the early maternity blues to postpartum psychosis, a serious state affecting <1% of mothers and usually requiring hospitalization [3]. Along this spectrum is postpartum depression (PPD) [4]. According to the *Diagnostic and Statistical Manual of Mental Disorders*, *Fourth Edition* (DSM IV-TR) [5], PPD symptomatology does not differ from the symptomatology in non-postpartum mood episodes and may include psychotic features. A fluctuating course and mood lability may be more common in postpartum episodes. When delusions are present, they often concern the newborn infant (e.g., the newborn is possessed by the devil, has special powers, or is destined for a terrible fate). In both the psychotic and nonpsychotic presentations, there may be suicidal ideation, obsessional thoughts regarding violence to the child, lack of concentration, and psychomotor agitation. Women with postpartum major depressive episodes often have severe anxiety, panic attacks, spontaneous crying long after the usual duration of "baby blues" (i.e., 3–7 days postpartum), disinterest in their new infant, and insomnia (more likely to manifest as difficulty falling asleep rather than as early-morning awakening) [5].

PPD is experienced by 10–20% of women who have recently given birth [6]. However, only a small proportion

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of these women are diagnosed as depressed [7]. Hearn reported that up to 50% of all cases go undetected [8]. This finding emphasizes the need for early diagnosis and treatment of PPD [9].

Depression is common in the population with chronic epilepsy [10,11]. The prevalence of depression in patients with epilepsy has been shown to range between 9% and 55% depending on the sample population and the method of assessment [12]. In contrast, in the general population, the prevalence of depression is thought to be 2–9% in women and 1–3% in men [13]. Women are more vulnerable to depression than men [14]. Recently, Blum reported a lack of gender difference in the prevalence rates of depression in patients with epilepsy [15]. Several factors are correlated in the development of depression in patients with epilepsy, such as etiology, seizure type, seizure frequency, antiepileptic drugs (AEDs), genetic susceptibility, and psychological and social factors [16,17].

As we have mentioned, a history of depression is significantly more frequent in patients with epilepsy compared with subjects without epilepsy. For this reason, our purpose in the present work was to investigate the relationship between epilepsy and PPD, because little is known about this topic. Our hypotheses were that women with epilepsy have a higher rate of PPD than women without epilepsy, and that clinical variables (type of epilepsy, duration and age at onset of epilepsy, seizure frequency, etiology of epilepsy, monotherapy or polytherapy) may influence the rate of PPD. To verify these hypotheses, we administered a clinical interview and a self-reported scale to assess PPD and to investigate the rate of PPD in patients with epilepsy and healthy controls. The goal was to determine whether there is a difference in the rate of PPD between patients with epilepsy and healthy controls and to correlate PPD with clinical variables in the population with epilepsy.

2. Methods

The study was performed at the University of Milan, St. Paolo Hospital. Between 1 April 2004 and 31 July 2005, 35 consecutive pregnant women followed at the Epilepsy Center were enrolled.

Inclusion criteria were: diagnosis of focal or generalized epilepsy made on the basis of anatomo-electroclinical criteria (previous clinical history, MRI findings, and EEG or video/EEG recording) according to the International League Against Epilepsy (ILAE) [18]; age at least 18; gestational age between 5 and 8 weeks; education level $\geqslant$8 years; and ability to read, understand, and speak Italian. Patients receiving medication other than AEDs and patients with a psychiatric background were excluded. None of the patients had previously experienced mood and anxiety disorders.

Thirty-five women without epilepsy were recruited at the Department of Obstetrics and Gynecology. The control group was chosen to match the patients with respect to age and education. Inclusion criteria for the control group were: age at least 18; gestational age between 5 and 8 weeks; education level $\geqslant$8 years; and ability to read, understand, and speak Italian. Women receiving medication and those with a psychiatric history were excluded.

All inclusion and the exclusion criteria for the patients with and without epilepsy were chosen to obtain a homogeneous sample of patients.

We recruited all patients at a gestational age between 5 and 8 weeks and performed the first clinical interview to exclude patients with a psychiatric background and patients receiving medication other than AEDs. We evaluated the psychiatric background with a clinical interview on the basis of DSM IV-TR [5]. It comprised past and current medical history and details on medicines taken by the women. At 5 to 8 weeks postpartum, all women completed the Edinburgh Postnatal Depression Scale (EPDS) [19], a second clinical interview, and a sociodemographic questionnaire.

All patients and controls gave their written informed consent prior to completing the questionnaires.

The Committee for Medical Ethics of Health of St. Paolo Hospital approved this study.

2.1. Questionnaires

2.1.1. Edinburgh Postnatal Depression Scale (EPDS)

EPDS is a 10-item (scored on a scale of 0–3) self-reported scale used to screen for PPD. Respondents were instructed to complete the EPDS based on how they had felt over the preceding 7 days [19,20].

The EPDS Italian validation suggests a 9/10 cutoff for its use in community surveys and screening and a 12/13 cutoff for clinical assessment. At the 9/10 cutoff score, the sensitivity is 83.3%, the specificity 89.5%, and the positive predictive value (PPV) 58.6% [21].

The EPDS is not a substitute for this clinical assessment, and a score just below the cutoff should not be taken to indicate the absence of depression, especially if the health professional has other reasons to consider this diagnosis. The data from the Italian validation suggest that a threshold of 9/10 might be appropriate if the scale is considered for routine use by primary care workers.

In our study, we used a 9/10 cutoff.

2.1.2. Clinical interview

We used a semistructured clinical interview to enroll patients with the inclusion and exclusion criteria selected. It was administered by a trained clinician and included the major axis I and II diagnostic classes [5]. In the first clinical interview (gestational age between 5 and 8 weeks) we assessed, on the basis of DSM-IV-TR criteria, clinical syndromes including schizophrenia and other psychotic disorders, mood disorders, anxiety disorders, attention disorders, somatoform disorders, other substance-related disorders, eating disorders, sleep disorders, and personality disorders of axis II [5]. The interview covered past and current medical history and details on medicines taken by the women.

Five to eight weeks after childbirth, we evaluated the women for PPD. The diagnosis of PPD was made by an interviewer using both the EPDS score with a 9/10 cutoff and a diagnostic interview according to the DSM-IV-TR [5,22].

2.1.3. Sociodemographic questionnaire

The sociodemographic questionnaire was used to collect information such as age, current employment status, marital status, years of education, and participation in prepartum training.

2.2. Statistics

Data are presented as means $\pm$ SD. Age and education of patients with epilepsy and controls were compared with the Mann–Whitney test. Marital status (married, with partner, and divorced) was compared with a one-way ANOVA. Differences in the number of children (primiparous vs multiparous) and in the number of vaginal deliveries between the two groups were analyzed with the χ^2 test.

To investigate differences in the mean EPDS score between the epilepsy group and the controls, we analyzed EPDS scores with the two-tailed Student t test for unpaired samples. EPDS scores presented a normal distribution. Multiple linear regression analysis was performed to determine the interaction between demographic and clinical variables, on the one hand, and the psychological test scores, on the other hand. The following variables were analyzed: age, education, type of epilepsy,

duration and age at onset of epilepsy, seizure frequency, etiology of epilepsy (probably symptomatic or symptomatic), monotherapy or polytherapy. The EPDS score was the dependent variable. A stepwise selection procedure was used with the α to enter set at 0.05 and the α to remove set at 0.10. Significance was set at a P value of 0.05. The results were analyzed using the Statistical Package for Social Sciences for Windows (SPSS 13.0).

The sample size was calculated by our Department of Statistics and Biometry, taking into consideration different variables (confidence interval, confidence level, and percentage of population with epilepsy).

3. Results

Clinical characteristics of the patients with epilepsy and demographic characteristics of the two groups are reported in Tables 1 and 2.

Table 1
Clinical characteristics of the patients ($N = 35$)

Type of epilepsy	
Generalized epilepsy	18 (51%)
Focal epilepsy	17 (49%)[a]
Probably symptomatic	4 (23%)
Symptomatic	13 (77%)
Seizure frequency	0.7 ± 1.7
Minimum/maximum	0/7
Duration of epilepsy (years)	18.8 ± 10[b]
Age at onset of epilepsy	13.7 ± 8.3
AED therapy	
Monotherapy	27 (72%)
Polytherapy	7 (24%)
No therapy	1 (4%)
Carbamazepine	12 (44%)
Valproate	7 (26%)
Phenobarbital	4 (14%)
Clobazam	1 (4%)
Ethosuximide	1 (4%)
Lamotrigine	1 (4%)
Oxcarbazepine	1 (4%)

[a] Number (%) of patients/controls.
[b] Mean ± SD.

Table 3 lists the mean EPDS scores for the patients with epilepsy and the control group. There were no significant differences in age (Mann–Whitney $U = 291.5$, $P > 0.05$), education (Mann–Whitney $U = 279.5$, $P > 0.05$), marital status ($F = 0.785$, $P > 0.05$); parity (primiparous: $\chi^2 = 0.022$, $P > 0.05$; multiparous: $\chi^2 = 0.360$, $P > 0.05$); or vaginal delivery ($\chi^2 = 0.831$, $P > 0.05$) between the patients with epilepsy and the controls.

The 35 women with epilepsy had a mean EPDS score of 7.0 ± 4.3 (range: 0–20), whereas the mean EPDS score in the women without epilepsy was 3.6 ± 3.4 (range: 0–14). Patients with epilepsy had a higher prevalence of symptoms of depression compared with the control group. The results suggest that there is a significant difference between the epilepsy group and controls with respect to PPD ($P < 0.05$). PPD was present in 29% of the patients with epilepsy and 11% of the controls.

The results of the multiple linear regression analyses, in which the association of EPDS with demographic and clinical variables was explored, are not statistically significant. EPDS scores were not associated with age, education, type of epilepsy, duration of epilepsy, age at onset of epilepsy, seizure frequency, etiology of epilepsy, or monotherapy or polytherapy.

None of our patients with and without epilepsy had premature births, intrauterine growth impairment, operative deliveries, or admission to neonatal care units. None of our patients' children with and without epilepsy had any malformations or minor anomalies, which may cause depression [23,24].

4. Discussion

The intent of this pilot research was to provide preliminary data on this topic. The design of this study provided a unique opportunity to compare the rate of PPD during the high-risk postpartum period in a population with epilepsy with that of a population without epilepsy. A primary finding of our investigation is the higher percentage of PPD in patients with epilepsy versus controls ($P < 0.05$).

Table 2
Demographic characteristics of the patients and controls

	Patients ($N = 35$)	Controls ($N = 35$)	Statistical test	P
Age (years)	32.5 ± 5.3[a]	31.8 ± 4.0	$U = 586.5$[b]	0.759
Education (years)	12.4 ± 3.5	13.5± 2.9	$U = 484.5$	0.119
Marital status				
Married	31 (89%)[c]	29 (83%)	One-way ANOVA 0.785	0.379
With partner	4 (11%)	5 (14%)		
Divorced	0	1 (3%)		
Primiparous	23 (66%)	22 (63%)	$\chi^2 = 0.022$	0.881
Multiparous	12 (34%)	13 (37%)	$\chi^2 = 0.360$	0.549
Vaginal delivery	26 (74%)	33 (95%)	$\chi^2 = 490.0$	0.21

[a] Mean ± SD.
[b] Mann–Whitney U.
[c] Number (%) of patients/controls.

Table 3
Mean EPDS scores of patients and controls

EPDS score	Patients ($N = 35$)	Controls ($N = 35$)	Statistical test	P
Mean ± SD	7.0 ± 4.3	3.6 ± 3.4	$t = 3.7$	0.001
0–1	4 (11%)[a]	8 (23%)	$\chi^2 = 1.33$	0.248
2–4	6 (17%)	18 (52%)	$\chi^2 = 6.0$	0.014
5–9	15 (43%)	5 (14%)	$\chi^2 = 5.0$	0.025
>9	10 (29%)	4 (11%)	$\chi^2 = 2.571$	0.019

[a] Number (%) of patients/controls.

Among the demographic and epilepsy-related variables, age, education, type of epilepsy, duration and age at onset of epilepsy, seizure frequency, etiology of epilepsy, and monotherapy or polytherapy were not associated with PPD in our group of women with epilepsy. Our correlation design does not allow for definitive conclusions regarding the causal relationship between PPD and clinical variables, although those findings would suggest that our sample is composed of a mild neurological phenotype.

Depression in pregnancy has been associated with premature births, intrauterine growth impairment, operative deliveries, and admission to neonatal care units [25]. Women with a previous history of depression have a 25% risk of recurrent depression after delivery [26]. None of our patients had a history of depression.

Although some studies have looked at possible etiologies, including hormonal fluctuation, biological vulnerability, and psychosocial stressors, the specific etiology of PPD remains unclear [27,28].

Identification of risk factors for PPD can guide intervention [29]. The severity of symptoms and the degree of impairment guide the approach to treatment. Treatment of PPD includes psychotherapy and pharmacotherapy [30]; many patients benefit from concomitant treatment with both of these approaches [31]. The efficacy of psychotherapeutic interventions for the acute treatment of PPD is strongly supported by empirical data, which suggest that counseling is of benefit as a stand-alone treatment for PPD [32]. PPD demands the same pharmacological treatment as does major depression, with doses similar to those given to patients with nonpuerperal depression [33].

Different authors have reported moderate to large adverse effects of PPD on maternal–infant interaction during the first year after delivery [34–36]. Compared with mothers who were not depressed, those with PPD displayed less affectionate behavior, were less responsive to their infants, and were withdrawn with flatness of affect. Infants whose mothers were depressed tended to be fussier and make fewer positive facial expressions and vocalizations than infants of mothers who were not depressed [37,38].

The quality of life experienced by these women and their families may be compromised [39,40]. Mothers experience fear and confusion; they suffer in silence because PPD has not been diagnosed. It is particularly difficult for women with new infants to disentangle symptoms of depression, such as fatigue, early-morning awakening, or weight loss, from the normal adaptation to life with a new infant [41].

The majority of women with epilepsy will have a normal pregnancy and delivery, an unchanged seizure frequency, and a greater than 90% chance of a normal baby [42].

Women with epilepsy have many concerns regarding the effects of their condition and the use of AEDs on their offspring. These concerns fall into four areas: increased seizure frequency, risk of birth defects, risk associated with breast feeding, and psychomotor problems associated with AED use [43]. These risks can be minimized with appropriate psychological counseling [44].

This study had a number of limitations. Our results should be interpreted with caution before the study is replicated with a larger sample: the overall small size of our sample restricts generalizations. The patients with epilepsy are heterogeneous and have different characteristics. Also, the association between epilepsy and mood disorders must be deeply investigated to better explain the interaction between biological, psychological, and social factors. Finally, we did not find any strong relationship between PPD and clinical variables. This issue needs to be more thoroughly investigated to verify an association between PPD and epilepsy, as well as some possible etiologies.

Our preliminary results suggest that the occurrence of PPD in patients with epilepsy deserves further examination and that new studies are necessary to support our data. Prospective studies including repeated assessment of PPD and the mother–child relationship may provide the complementary information required to determine the health needs of women depressed in the postpartum period and their children.

In summary, we confirm the importance of a PPD assessment, and our findings offer a starting point for further investigations on larger samples to obtain clearer and more reliable results. Although PPD symptoms are frequently observed in women with epilepsy, they are often underrecognized and undertreated. Increased awareness on the part of clinicians may help to develop effective prevention and intervention strategies to improve long-term outcome and quality of life.

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