

Recent epidemiologic studies have found that most patients with mental illness are seen exclusively in primary care medicine. These patients often present with medically unexplained somatic symptoms and utilize at least twice as many health care visits as controls. There has been an exponential growth in studies in this interface between primary care and psychiatry in the last 10 years. This special section, edited by **Jürgen Unutzer, M.D.**, will publish informative research articles that address primary care-psychiatric issues.

Risk factors for early postpartum depressive symptoms[☆]

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Abstract

Objective: Postpartum depressive disorders are common and symptoms may appear as early as the first 2 weeks postpartum. Data regarding hormone-related risk factors for depressive symptoms occurring in the very early postpartum period are scarce and may be of importance in identifying serious postpartum illness. We examined the association between the reported history of psychiatric symptoms of possible hormonal etiology and very early postpartum depressive symptoms.

Methods: All women ($n=1800$) in a general hospital maternity ward were assessed during the first 3 days after parturition for potential risk factors for postpartum depressive disorders by a self-reported questionnaire and for present mood symptoms (Edinburgh Postnatal Depression Scale, EPDS). The associations between potential risk factors and postpartum depressive symptoms were analysed.

Results: The incidence of women with an EPDS ≥ 10 was 6.8% (88/1286). Significant risk factors for early postpartum depressive symptoms were a history of mental illness including past postpartum depression (PPD), premenstrual dysphoric disorder (PMDD), and mood symptoms during the third trimester.

Conclusion: In accordance with other studies, a history of depression was found to be a risk factor for early postpartum mood symptoms. An association was also found between some risk factors of possible hormone-related etiology such as PMDD and third trimester mood symptoms and early postpartum mood symptoms. As such, early postpartum symptoms may indicate vulnerability to subsequent PPD; it may be of importance to assess these risk factors and mood immediately after parturition. A prospective study is needed to determine which of these risk factors is associated with progression to PPD and which resolves as the blues.

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1. Introduction

The prevalence of postpartum depressive disorders is 10–15% for depression (major or minor) and as high as 50–80% for the “blues” [1,2]. Postpartum depression (PPD) is sometimes associated with severe emotional suffering and may involve actual risk to the mother and baby [3,4]. Furthermore, through interference with attachment processes and

possibly other factors, postpartum depressive disorders have a negative effect on the development of the baby [5]. Despite their commonness, up to 50% of the cases of postpartum disorders go undiagnosed or treated [6]. While most cases of PPD develop after the first 2 weeks postpartum, there is evidence that depressive symptomatology increases as early as the first 2 weeks postpartum [7], and that in women at risk, a considerable percentage may develop PPD during this period [8]. Thus, knowledge of risk factors that predispose women to early postpartum depressive symptoms may enhance early identification of those who require professional help for prevention or successful early treatment [9].

A number of risk factors have been associated with the development of PPD. These findings are not always conclusive and are reviewed elsewhere (e.g., Refs. [1,10,11]).

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While the blues is a well-established risk factor for PPD [4,11,12,13], little data exist regarding other syndromes that may reflect individual hormonal sensitivity such as premenstrual dysphoric disorder (PMDD) [4,14], psychiatric symptoms during pregnancy [15,16], mood instability secondary to oral contraceptives [17,18], or mood instability at puberty [19,20]. Despite the paucity of data, researchers in the field have hypothesized that some women have emotional and physical sensitivity during such times of hormonal changes, making them prone to the development of depressive symptoms during vulnerable periods [20–22]. Risk factors related to personal history of mental illness such as affective disorder [23,24], PPD in the past [32] or a family history of depression [3,4] have been consistently found to be important risk factors for PPD.

In the present study, we used a retrospective design to examine possible risk factors for the development of early postpartum depressive symptoms, with an emphasis on factors that may reflect individual variations of hormonal sensitivity.

2. Methods

2.1. Study population

All women admitted to the Rambam Medical Center's (Haifa, Israel) two maternity wards during the years 1998–1999 were consecutively assessed for this study. Inclusion criteria were fluency in Hebrew and willingness to sign the informed consent. Two research assistants approached all newly admitted women to the two maternity wards 1–3 days postpartum. Compliant eligible women completed a questionnaire containing information regarding potential risk factors for PPD. Present mood was assessed with the Hebrew version of the Edinburgh Postnatal Depression Scale (EPDS) [25] and self-report questions regarding their mood.

Twenty-eight percent of the eligible women could not be assessed for technical reasons such as early discharge, continuous guest visits, medical procedures, etc. Only 1% of the women refused to participate. A total of 1800 women were administered the questionnaire after providing a written informed consent. Of these, 71% ($n=1286$) completed both the full questionnaire and the EPDS and were included in the analyses.

2.2. Risk factor questionnaire

The risk factor questionnaire contained the following information: (1) General demographic background. (2) Description of the present and past pregnancies. (3) Personal (major depression and other major diagnoses) and first-degree family psychiatric history. (4) past hormone-related mood symptoms: (a) Mood instability during puberty, considered positive only if causing severe distress. (b) PMDD, based on *DSM-IV* criteria, considered positive only if there were severe premenstrual emotional symptoms of sadness,

irritability, mood lability or anxiety that occurred during most cycles, starting in the luteal phase and ending with menses and causing considerable distress or functional impairment. (c) Emotional reactivity to oral contraceptives, considered positive if women reported of sadness, irritability, mood lability or anxiety while taking oral contraceptives leading to the termination of treatment. (d) Sadness, irritability, mood lability or anxiety occurring during the third trimester of the present pregnancy. (5) Present mood instability or depressive symptoms since parturition.

2.3. Edinburgh Postnatal Depression Scale

The EPDS is a 10-item questionnaire developed by Cox et al. [26] to detect PPD. The sum of the EPDS correlates with the severity of depression [27], and a score of 10 or above indicates high risk for developing PPD [23,28]. The EPDS has been translated to and validated in many languages, including validation in Hebrew [25]. While the EPDS was developed as a tool to detect PPD (not in the immediate postpartum period), its use has widened and it is now often used as a screening tool as early as the first few days of the postpartum period [10,11,29,30].

2.4. Statistical analysis

All women were divided into two groups: the symptomatic group with an EPDS score ≥ 10 and the asymptomatic group with EPDS scores < 10 . To ascertain that the study and comparison groups were indeed well matched, a set of t -tests (for continuous variables) and χ^2 analyses (for discrete variables) were used. The relationship between the various risk factors and EPDS score was assessed using a set of χ^2 analyses. One-way ANOVA was used for the analysis of continuous variables. We also applied a hierarchical regression model to the various risk factors to identify the optimal model for prediction of postpartum outcome.

3. Results

The average age of the study population was 30.6 (S.D.=5.7). Most of the study population were married

Table 1

The association between reported risk factors and EPDS scores of 10 and above during the early postpartum period

Past history risk factors		N	EPDS ≥ 10	P^a
Mood symptoms at 3rd trimester	Yes	325	22 (6.8%)	<.001
	No	908	14 (1.5%)	
PMDD	Yes	273	14 (5.1%)	.015
	No	971	22 (2.3%)	
Postpartum depression	Yes	13	5 (38.5%)	<.001
	No	1034	23 (2.2%)	
Other psychiatric illness	Yes	15	3 (20%)	.008
	No	1213	23 (2.7%)	
Affective disorders in family	Yes	141	8 (5.7%)	.048
	No	939	24 (2.6%)	
Major depression	Yes	24	2 (8.3%)	.150
	No	1196	34 (2.8%)	

^a Significance calculated using χ^2 tests.

Table 2

Logistic regression of risk factors predicting EPDS scores among women on their 1–3 postpartum day ($n = 1286$)

	R^2	Beta	Standard error	t	Significance
Model	.082				
Mood during pregnancy		−1.58	0.169	−9.4	.000
PMS		−.72	0.154	−4.6	.000
Past episode of major depression		−1.65	0.356	−4.6	.000

women (96%) and of average or above economic status (77%). Number of live children at home was 1.26 (S.D. = 1.3). There was no significant difference in demographic factors between the two groups of women when divided according to EPDS score. Of the 1800 women screened, 1286 women (71%) fully completed the questionnaire and were used for the risk factor analysis. The incidence of symptomatic women (EPDS ≥ 10) when assessed between Days 1 and 3 postpartum was 6.8% (88/1286).

3.1. Risk factors that were found to be significant predictors of postpartum depressive symptoms

Table 1 presents the incidence of an EPDS score of 10 or above (representing significant postpartum depressive symptoms), in women with or without various risk factors. Risk factors that were found to be significantly associated with postpartum depressive symptoms are (1) a history of mental illness (a past history of PPD, other depression or other psychiatric illness and a family history of affective disorders), and (2) hormonal factors (PMDD and mood symptoms during the third trimester of pregnancy).

The following factors were not found to be associated with postpartum depressive symptoms: economic status, marital status, ethnic background, number of children, planned vs. unplanned pregnancy, spontaneous pregnancy vs. hormonal treatment or IVF, type of birth (normal labor or cesarean section), mood symptoms secondary to oral contraceptives and mood instability at puberty.

Applying a hierarchical regression model (selection method = R^2) to the various risk factors, we determined three risk factors included in the optimal model for prediction of postpartum outcome — mood instability at third trimester, past depression and PMDD, accounting for only 8% of the variance in EPDS (Table 2).

4. Discussion

In this work, we assessed the possible association between different risk factors and early postpartum depressive symptoms in a healthy population.

4.1. Prevalence of postpartum depressive symptoms

The EPDS questionnaire is widely used for the assessment of current mood and postpartum depressive symptoms both in the early (3–5 days) and late (1–3 months) postpartum periods

[7,8,31,32], and as a measure for PPD in the assessment of possible risk factors [16,33]. An EPDS cutoff score of 10 is commonly used as an indication for clinically significant PPD [11,26]. In previous studies of early postpartum symptoms, Lane et al. [31] found that 11.4% of their sample of women had an EPDS score of 13 and above 3 days postpartum, and Bergant et al. [32] found that 20% of women had an EPDS score of 10 and above 5 days postpartum. As of the “blues”, many studies report its prevalence as high as 50–80% [2]. In the present work, a relatively low incidence of symptomatic women with an EPDS score of ≤ 10 was found (6.8%). This may have two reasons: First, the fact that the chosen EPDS cutoff score of ≥ 10 is usually associated with clinical depression rather than mild mood symptoms as would be expected to emerge in the first days postpartum. Second, in the present study many of the women had been screened before the third day postpartum, while depressive symptoms as part of the postpartum blues are usually expressed 3–7 days postpartum [2]. Thus, we may not have identified all women who subsequently did develop early postpartum depressive symptoms in the next few days.

4.1.1. Risk factors for postpartum mood disorders

4.1.1.1. Mood symptoms at third trimester. Pregnancy has traditionally been conceptualized as a period of increased well-being and emotional stability [34]. However, Dean et al. [35] reported that 50% of women with postpartum psychiatric symptoms had depressive symptoms during pregnancy. O'Hara et al. [36] also reported that depressive symptoms during pregnancy predicted the onset of postpartum blues. Recently, prospective studies have shown that the rate of depression may be similar during pregnancy and the postpartum period, and that the presence of anxiety or depression during pregnancy is associated with depressive illness during the puerperium [15,16,37,38]. The results of the present study support the notion that third trimester mood symptoms predict subsequent depressive symptoms in the early postpartum period as well.

4.1.1.2. Premenstrual dysphoric disorder. While prospective studies are lacking, existing data from uncontrolled studies support the hypothesis of an association between PMDD and the development of PPD. Pearlstein et al. [14] reported that 78% of women with PMDD will develop an axis I disorder during their lifetime, and 69% of them will develop depression. In addition, 29% of the parous women interviewed, who also met criteria for PMDD, had a prior episode of minor or major PPD. This figure is two times higher than prevalence of PPD as reported in the *DSM-IV* (8–12%) and is compatible with the incidence rate of 23% PPD we have found in a prior work in women with PMDD [39]. In another study, 68% of a group of prospectively confirmed PMDD patients reported a history of PPD. Similarly, high postpartum depressive scores have been associated with a history of PMDD [17,40,41]. The relation of PPD to the menstrual

cycle is also supported by a report by Brockington et al. [42] who found higher depressive scores in women with PPD during the days before menses. In the present study, women who had PMDD in their past developed significantly more early postpartum depressive symptoms than women without PMDD, further supporting the notion of a common diathesis for PMDD and PPD. While the retrospective diagnosis of PMDD is considered relatively less reliable, we have used the *DSM-IV* criteria, which were operationalized, and only considered positive if all criteria were met and the symptoms were severe, thus limiting the possibility of memory bias. This method has been advocated as a useful and practical screening method for PMDD in a recent article by Steiner et al. [43].

4.1.1.3. Past history of PPD. Many studies found an association between PPD in the past and a current episode of PPD [4,33] and only a few did not [16]. According to Garvey et al. [24], the probability to develop a PPD in women with PPD in the past is 75%. Another study found that women with past PPD without psychotic symptoms have a 30–50% probability to develop PPD in their next pregnancy [23]. The chance to develop postpartum psychosis in a woman with a history of postpartum psychosis in the past is 1:3–1:7 [2]. Our study is in line with the existing data in that a past history of PPD was found to be strongly associated with early depressive symptoms.

4.1.1.4. Past history of major depression or other psychiatric illness. Most studies [16,23,44], but not all [3,12], have found a personal history of affective disorder to be a strong risk factor for PPD and for an exacerbation of symptoms [45]. The chance to develop postpartum psychosis or depression in women with a past history of an affective disorder is between 1:5 [2] and 1:3 [24,27]. In the present work, our results are consistent with the existing literature, although due to the small number of women who reported an episode of past major depression, the association of postpartum depressive symptoms with a history of depression does not reach statistical significance.

4.1.1.5. Family history of affective disorders. Family history of depression was found to be associated with PPD in prospective, retrospective and sectional studies [2,4]. Jones and Craddock [46] found that familial factors are implicated in the susceptibility to the triggering of puerperal episodes in women with bipolar disorder. Other studies found no such association [3,23]. In the current study, the prevalence of women with a family history of affective disorder, who had an EPDS score of ≥ 10 , was significantly higher than in women with no family history.

4.1.2. Conclusion

We assessed the role of various risk factors for the development of early postpartum depressive symptoms with an emphasis on factors that are presumably hormone-related.

While psychosocial and obstetric factors were not found to be associated with early postpartum depressive symptoms, a history of PMDD, depressive symptoms during pregnancy and psychiatric history — personal or familial — were found to be associated with such symptoms. While there is much data implying that hormonal changes are critical to the development of PMDD, depressive symptoms during pregnancy may actually reflect fear of delivery, lack of sleep, concerns about parenting, physical discomfort and more, and thus may not be hormone-related. As early postpartum mood symptoms may indicate vulnerability to subsequent PPD, these risk factors should receive attention in screening for women at risk for PPD. However, as this study did not attempt to differentiate between the “blues” and early mood symptoms that may precede PPD, and since the prevalence of PPD is a rather small fraction of the self-limiting “blues”, the use of early symptoms in a screening program for PPD is limited by the fact that it would lead to high rates of false positives. Furthermore, other potential events that may theoretically induce mood change secondary to hormonal factors, such as puberty and the use of oral contraceptives, failed to show an association to postpartum mood in the present study. These factors may be very weak risk factors which could not be identified by the design of the present study, or, alternatively, do not have a role in predicting sensitivity to early postpartum mood changes.

The present study is limited by the fact that the information regarding risk factors was acquired retrospectively by self-report and is thus prone to memory bias. It is possible that women who were more symptomatic tended to recall past mood symptoms at a higher frequency. Furthermore, the lack of structured interviews limits our conclusions to depressive symptoms and not to specific psychiatric diagnoses.

We have previously shown that women with a history of PPD have a differential vulnerability to gonadal steroids compared to women without a history of PPD [47]. While the biological basis for this differential sensitivity is still unknown, it may represent the effect of genetic polymorphism in genes that regulate reproductive hormone signaling or that are regulated by reproductive hormones, predisposing some women to detrimental mood effects of gonadal steroids. While the associations presented in this study do not imply causality, the results further support existing epidemiologic data linking the predisposition to PPD with other putatively hormone-linked phenomena. This association is suggestive of an increased vulnerability to the mood-destabilizing effects of reproductive hormones in a subgroup of women, a phenomenon consistent with the onset of mood disorders during either pregnancy or the postpartum. Furthermore, this association emphasizes the importance of biological factors in the etiology of postpartum depressive disorders, an area that should be further explored. Interestingly, a similar association has been found between perimenopausal depression and hormone-related phenomena such as oral contraceptive dysphoria, PMDD, postnatal blues and PPD [48]. Thus, women who suffer from affective disorders following

one reproductive event may be more vulnerable to recurrences associated with others. While yet to be definitely proven, the theory that hormonal factors have an important role in the etiology of PPD is not only important for further research, but also is helpful clinically as it is a socially acceptable explanation for depression, which is highly stigmatized, especially after the birth of a healthy baby.

As the risk factors found here explain only 8% of the diversity seen, other unaccounted etiological factors must be involved in the development of postpartum mood disorders. Such factors could be general biological vulnerability to depression (e.g., serotonergic dysregulation), psychosocial support (e.g., family bonds) or psychological factors (e.g., coping mechanisms), and these should be further explored. To determine the clinical importance of these findings, a prospective study is needed to determine which of these risk factors is associated with progression to PPD and which resolves as the blues.

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