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Chapter 5: Addressing postpartum depression through hormonal, psychological, and pharmaceutical lenses

5.1. Introduction

Postpartum depression (PPD) is a severe but under-recognized disorder that affects about 10-30% of postpartum females, depending on their specific risk factors. Research about PPD has pointed toward various hormonal, psychological, and pharmaceutical models as explanations for its occurrence. Typically associated with mothers, recent evidence suggests that PPD is also likely to occur in fathers or other caregivers. For caretaking purposes, PPD could hinder a new mother's capacity to care for herself and meet her child's needs adequately, thus directly affecting her own and the child's livelihoods. Besides possibly compromising family health status, this disorder can be a heavy burden on the healthcare system – with negative consequences that further extend to the social and economic environments Alvarez et al., 2023; Kim et al., 2024; Reynolds et al., 2024).

PPD can be treated through psychotherapy, the use of antidepressant medication, or combined treatment; most cases are resolved by 3-6 months postpartum with these therapies. There is yet no consensus about the best treatment. Addressing PPD through the hormonal lens may focus on the changing reproductive hormones pre- and postpartum. Neurotransmitter activity may also be negatively impacted by the postpartum release of prolactin in conjunction with the suppression of the estrogen-testosterone axis, thus forming a biological link between hormonal action and mental health. Corking the excessive activity of the stress response axis has become a more novel but equally promising treatment approach: Decreasing glucocorticoid excess could also prevent adverse results of the cortisol-induced decrease of serotonin. Estrogen exercises a positive effect on serotonin, a neurotransmitter whose activity is reduced in

the pathogenesis of PPD: Several studies have found low levels of serotonin after delivery. The built-up feeling of worry leads to a state of distress and low mood: A reduced sensitivity to pleasant experiences further demotivates the individual to break the vicious cycle signified by negative mood symptoms. Other treatment avenues have been reviewed, too – mainly staff recommendations and psychotherapy – which still appear to be of utmost importance in postpartum treatment due to their influence on cortisol levels (Singh et al., 2023; Thompson et al., 2025).

5.1.1. Overview of the Topic

Postpartum Depression (PPD) is a psychiatric disorder within the postpartum period that affects approximately 10-15% of birthing individuals, however, prevalence rates may be twice as high in certain cohorts. It is characterized by strong feelings of sadness or anxiety, changes in sleep or energy, and impairment in daily functioning. PPD has been associated with both obstetrical and infant health consequences, and has ramifications for psychiatric sequelae beyond the transient postpartum period. Hormonal, psychological, and pharmaceutical causes of PPD have been noted, although what validates a disorder is unique to each individual and difficult to define. Addressing the question of "what causes PPD?" is difficult given the variability and subjective nature of experiences surrounding childbirth. It has been widely accepted that hormonal changes surrounding parturition trigger PPD, and indeed, animal studies have noted depressive-like behaviors postpartum due to a lack of hormonal recovery. However, PPD prevalence is higher in individuals with a history of mood disorders, and further, other psychological strains, such as lack of social support or high stress surrounding childbirth, have been associated with higher rates of PPD. Treatments for PPD have commonly been pharmacological, specifically using SSRIs, but recent concerns regarding the effects on breastfeeding and withdrawal symptoms in infants have encouraged studies of non-pharmaceutical interventions, including psychotherapy, exercise, meditation, and acupuncture. These studies have yielded mixed results.

Because of the overlap in causes of PPD, therapies targeting multiple areas of PPD may be more effective than singular treatments. In tandem, considering the major implications of PPD for both mothers and their children, further study of risk factors for PPD as well as effective treatments is needed. Current guidelines used to screen birthing individuals may overlook PPD in those who do meet specific criteria, so continued efforts to develop instruments for accurate screening are of utmost importance. Addressing the question of "what causes PPD?" is difficult given the variability and subjective nature of experiences surrounding childbirth.

5.2. Understanding Postpartum Depression

The perinatal period is a unique and delicate period in a woman's life, allowing for the formation of an important attachment to her newborn infant, as well as important milestones in the body and brain. Paradoxically, this greater vulnerability occurs alongside such a major biological accomplishment. Although it is a cause for celebration, the perinatal period brings great physiological, psychological, and interpersonal shifts that harbor great risk for the onset of psychiatric symptoms. Major depressive episodes are one of the most common psychiatric disorders in the perinatal period, with onset occurring during pregnancy or within the first few months of postpartum, and are associated with various adverse sequelae for both the mother as well as her growing child. Understanding the complexity of this condition can guide better screening, treatment, and referral pathways for these patients, and ultimately reduce maternal psychiatric disease burden.

Fig 5 . 1 : The Perinatal Paradox Joy and Vulnerability

Research suggests that nearly 1 in 5 women may suffer from perinatal depression, the onset of which can lead to major functional impairment and impaired bonding with the child. However, a large proportion of patients never seek help, partly due to stigma, shame, education, lack of healthcare access and integrated maternity care, or simply lack of time or resources. Perinatal depression can have many adverse effects on women, from dysphoria and disruptions to maternal-infant bonding to functional impairment and poorer relationship quality, and can also contribute to worsening obesity. These adverse effects are not limited to mothers themselves, but can also extend to the infants and

families. Untreated maternal depression can lead to developmental and behavioral difficulties in the offspring and may increase the risk of postpartum depression in subsequent pregnancies. It may also further increase the risk of psychiatric disorders in children later in life, including anxiety, depression, and substance use disorders.

5.2.1. Definition and Overview

Postpartum depression (PPD) is a complicated issue that arises in a woman after childbirth. The cause is unknown and could differ based on the woman and likely a combination of various factors. Nevertheless, most consider it to be an inflammatory reaction to the sudden drop in sex hormones, estrogen, and progesterone, after a woman gives birth. A woman affected by PPD could present physical, emotional, and behavioral symptoms that interfere with her ability to bond with her newborn baby or those around her. Such symptoms are typically not intuitive and women fail to get the proper intervention and treatment. PPD can come as a single incident, which can last weeks to months after delivery, can be recurrent over multiple pregnancies, or can start during pregnancy with prenatal depression. Without intervention, PPD can last longer than other mood disorders, can interfere with the relationship between the parent and the child, and might put the child at risk for developing behavioral and emotional issues. Furthermore, PPD can also be correlated to Birth-Related Post Traumatic Disorder, which is different than general stress during pregnancy or after delivery.

Most consider PPD to be an inflammatory reaction due to the hormonal imbalance that occurs after birth. However, more recently, researchers and scientists are looking at postpartum depression through a psychological lens as well as a pharmaceutical one. The psychological lens focuses more on the emotion and support of the mother. The mother goes through so many changes, physically and mentally, during and after pregnancy. These changes can impact a mother tremendously if she is not given the needed love and support from family and friends. The hormonal and psychological lenses are not mutually exclusive. There are women who after childbirth do not receive support and are predisposed to the inflammatory reaction; thus, it is understandable why researchers are questioning the lens through which postpartum depression should be assessed and treated. Other researchers are looking at postpartum depression through the pharmaceutical lens as they compare the efficacy of certain treatments versus placebo.

5.2.2. Prevalence and Impact

Postpartum depression (PPD) is the most common morbidity after childbirth, affecting several million women around the world. About 13 out of every 100 women experience PPD in the United States with a similar pattern found in other developed countries.

However, in lower-income countries such as China and India, the rates of PPD may be as high as 20-30%. While maternal deaths are rare due to advances in obstetric care, suicide is one of the leading causes of death during the first postpartum year. It is estimated that 1 out of 500 women who are diagnosed with PPD die by suicide. Several risk factors have been identified for the development of PPD including, for example, a history of depression, low levels of social support, partner conflict, and catastrophizing nature, which is the tendency to fret excessively. Low healthcare access is often an issue in low-income, high-PPD-prevalence countries. The lack of medical resources inhibits the education and treatment of PPD.

Long-term implications of PPD can be disastrous not just for the new mother but also for their children, families, and society as a whole. Women who suffer from PPD have a significantly greater chance of suffering from clinical depression years later. The effects, however, do not only last for the mothers and are seen in children showing adverse outcomes, including greater problems with mother-child interaction, more behavioral problems, worse cognitive development, and reduced communicative development at ages 2 and 3 compared to other mothers. High costs, including increased need for social, health, and educational services, crashes in the workforce, and dependency on social security support, are often incurred by society for many years thereafter about PPD.

5.2.3. Risk Factors

Postpartum depression (PPD) is a multifactorial disorder, and the presence of stressors or vulnerabilities, such as life events, low support, or experience of previous depression either during or after pregnancy, can influence its course. Gaps in knowledge and experience around PPD among women, partners, and healthcare professionals contribute to a lack of recognition and therefore a lack of support and treatment. There are many differences in the studies investigating risk factors for PPD after different childbirth problems. As a general rule, it is known that cesarean sections, operative vaginal childbirth, prolonged labor, and having a baby with problems, such as inability to suck, low weight, or need special care after birth, placed with abnormal neurological, metabolic, or other physical conditions, are risk factors. Current research has also found that suboptimal breastfeeding in particular, including healthcare provider-perceived failure to breastfeed properly, poor initiation, breastfeeding problems, or cultural discontinuity may increase the risk of PPD. Similarly, stopping to breastfeed too early, or having a more severe or chronic condition are also associated with PPD.

It is also suggested that single mothers or unplanned pregnancies may have significantly increased the chance of presenting PPD. Results from some other studies suggest that past treatment for depression should be emphasized in the obstetric patients' history, as

it may influence the development of PPD. Low socioeconomic status, unemployment, smoking, pregnancy complications, cesarean delivery, marital conflict, and bad maternal health or social support may also be important predictors of the disorder. Hence, several important risk factors for PPD may be addressed when screening for PPD. However, the majority of these factors, where applicable, would likely be intervened upon, making risk factor screening less critical with regard to enhancing PPD treatment, and other approaches may be more useful.

5.3. Hormonal Influences on Postpartum Depression

1. Role of Hormones

Surmounting evidence supports the involvement of fluctuating gonadal hormones in the etiology of postpartum depression (PPD), including the association between PPD and conditions of hormonal change, such as pregnancy and the postpartum period. Gonadal hormones—including estrogens and progesterone—have profound effects on multiple biological systems that are known to be disrupted in PPD, including the serotonergic, dopaminergic, and norepinephrinergic systems. The rapid decrease in estrogen and progesterone that occurs after childbirth exerts the largest impact on mood and behavior, emphasizing the importance of studying PPD in the context of hormonal transitional states. Moreover, women are uniquely endowed with periods of hormonal change where mood and behavior can rapidly change, including menstruation, pregnancy, postpartum, and menopause. However, our understanding of the role of hormones in mood disorders that occur during these periods is limited. Investigating the biological mechanisms underlying mood vulnerability during these hormonal transitions may aid in the development of novel hormone-based prevention and treatment strategies for PPD.

2. Hormonal Changes During Pregnancy and After Birth

Pregnancy is characterized by increasing concentrations of plasma estrogen and progesterone. Estradiol increases exponentially from the first trimester to the third trimester of pregnancy until a peak occurs during the late third trimester. A rise in serum estrone also occurs during late pregnancy, particularly in the third trimester compared to the nonpregnant state. The estradiol and estrone concentrations rapidly decline within the first few days after birth, while the levels of estriol, which increases during the second trimester of pregnancy, rapidly decline after parturition. Likewise, plasma progesterone rises exponentially during pregnancy reaching levels that are approximately 15–100 times greater than that of the nonpregnant state. The plasma progesterone concentrations also rapidly decline following childbirth.

5.3.1. Role of Hormones

Around 2 weeks postpartum, 1 in 7 women experience postpartum depression (PPD), characterized by lack of motivation, focus, and enjoyment, as well as poor sleep and appetite, feelings of shame and worthlessness, and difficulty bonding with the child. While these symptoms can arise from several physical, emotional, and environmental stressors, they are especially pronounced when women have a pre-existing history of clinical depression. PPD is most prevalent in the United States, followed by the introduction of transient but extreme drops in estrogen and progesterone. Given how effective hormonal replenishment has been for other disorders relating to low hormonal states, researchers have speculated whether similar physiological states existed in PPD and have investigated hormonal interactions with a number of pharmacological and psychological protective factors or therapeutic targets.

The first clue as to the role of hormones was the discovery of menorrhagia during postpartum repair. While menorrhagia is often caused by endometrial dysfunction, other possible causes include thyroid disease, luteal phase defect due to a deficiency in the luteal phase or corpus luteal function, or decreased cortisol. All of these possible causes share fluctuating or decreased levels of P4 or are associated with decreased levels of P4, as well as the presence of an estrogen-dominant state in the presence of hypothyroidism. A decrease in P4 levels has also been correlated with both endometrial dysfunction and PPD. Additionally, postpartum ovaries also have decreased steroidogenesis and luteinization and exhibit increased follicular atresia compared to pre-pregnancy ovaries. Since P4 withdrawal has been implicated in PPD, these findings would suggest that PPD develops from a hormonal withdrawal following delivery. Therefore, this led researchers to investigate whether a physiological state resembling PPD accompanied P4 withdrawal or low P4.

5.3.2. Hormonal Changes During Pregnancy and After Birth

Pregnancy is a time full of altered hormone levels, experienced both acutely and chronically. There is a delicate balance of hormones required for a successful pregnancy. Gonadal hormones are essential, however, other hormones such as human chorionic gonadotropin, human placental lactogen, insulin, and thyroid hormones are also vital for establishing and maintaining a pregnancy. Estrogen and progesterone levels are stable during the initial period of pregnancy, the first trimester, then gradually increase throughout the second and third trimesters in order to prepare the body and brain for labor and delivery. Following birth, all these hormones rapidly drop to pre-pregnancy levels, other than the breast-promoting hormones, which take considerably longer to return to baseline levels. The relatively fast decrease in gonadal hormone levels

postpartum occurs because the placenta, which produces these hormones acutely during pregnancy, no longer is in the body.

While we often consider during pregnancy the maternal body adjusting to the increasing fetal demands, we also need to consider the fetal response to fluctuating maternal hormone levels. There is a clear evolutionary advantage to coordinating at least some aspects of fetal development with maternal hormone levels, for example, ensuring lung development just before the maternal hit of cortisol and stress at the time of delivery. However, there is still so much to understand, including as it relates to postpartum depression.

5.3.3. Biological Mechanisms

Although the hypothesis of the etiology of PPD linked to changes in gonadal hormone secretion related to childbirth came to the fore thanks to clinical observations, reporting the incidence of symptoms of mood disorder in mothers who had recently given birth, filled with the notion that it would be a form of premenstrual depression exacerbated by pregnancy and postpartum hormonal fluctuations, and also to treatment responses with techniques insisting on fluctuation and/or depletion in estrogen levels, the observation of the efficacy of specific antidepressant treatments suggested that this clinic was subtended by the same biological and genetic basis as the other types of affective disorders. The neurotrophic hypothesis of affective disorders ponders that there is a decrease in levels of BDNF of neurotrophin and other neurotrophic factors in affective disorders. Hormones fluctuate during the menstrual cycle, especially considering the variations of their values in the postpartum period, and this fluctuation is capable of varying BDNF levels, enhanced by estrogens, especially estradiol. In animal models, the induced depletion of BDNF led to the development of an affective disorder profile. Other neuroinflammatory and neuroimmune markers are associated with affective disorders and behavior, in particular M1 proinflammatory polarization markers associated with cytokines. Studies in pregnant women presented data that suggest that women with a history of PPD had an increase in proinflammatory markers and a decrease in anti-inflammatory markers, during the postpartum period which could bring an increase in the incidence of PPD in these women. New studies are needed, especially in an attempt to understand the specific postpartum profile of vulnerable women, for specific follow-up, and to determine the exact moment of the treatment's beginning, considering the new datasets.

5.4. Psychological Perspectives

Despite being termed "baby blues," it is clear that postpartum depression cannot be merely reduced to 'a degree' of a positive consequence experienced by the vast majority of women having recently given birth to a child. The range of negative emotional consequences experienced, and the degree of impairment it can produce in a woman's life, vary considerably from individual to individual, and some report experiences so debilitating that they need to continue in therapy or undergo medical treatment long after the postpartum period is over. It is entirely understandable that a woman's emotional response to the postpartum experience may be quite different than the rejoicing of friends and family expected by the culture at large, if for no other reason than some women may be experiencing a very real sense of loss rather than celebration—a loss of a competent sense of self, freedom from the demands of the infant, loss of intimacy within the bond of sexual partnership, and the loss of the uncomplicated inevitability of physical life stages. The following section examines the lens of psychological perspectives through which postpartum depression is viewed.

Cognitive Behavioral Factors

Cognitive-behavioral theory has provided one of the more influential models for the study of normal and abnormal emotional experiences within women. Based on the cognitive theory of depression, postpartum women's irrational automatic thoughts are focused on their competence to take care of their baby and feelings of unworthiness about who they are as individuals as well as a view of the world as one that is rejecting might occur. These irrational thoughts act as mediators between stress generated by the activity of rearing an infant and the experience of depression. Their presence and hyperactivity when caring for an infant may produce low self-esteem and a negative self-image.

5.4.1. Cognitive Behavioral Factors

Understanding the cognitive behavioral factors that contribute to postpartum depression (PPD) is essential for the accurate diagnosis and treatment of mothers suffering from the disease. Cognitive theories postulate that cognitive distortions may be a significant feature of PPD, particularly rumination and negative cognitive set. One way of considering these cognitive-behavioral factors is to conceptualize PPD as depression occurring in women with a previous history of depression who may have cognitive vulnerabilities predisposing them to react with maladaptive thinking styles to the specific challenges and pressures of early motherhood. Definitions of PPD therefore include the occurrence of a constellation of cognitive, behavioral, emotional, and physical symptoms; alongside culturally determined expectations of maternal behavior and

psychological processes associated with the transition to motherhood. In many Western cultures, the expected experience of motherhood is infused with a combination of emotional joy and fulfillment. Many new mothers, however, have found this experience disrupted by the onset of extreme periods of emotional distress, and the feelings of anxiety and sadness are often experienced at a time when they are expected to be feeling the happiest and most fulfilled. Some studies have demonstrated that mothers' expectations of the emotional experience of motherhood are lower than those of their partners, and this difference has been associated with emotional distress in new mothers. Most mothers will experience some negative emotional reactions, such as sadness, anxiety, or negative thoughts about themselves and their new baby, during pregnancy and in the postpartum period. These emotions can feel overwhelming and lead to serious problems, such as disruption of the baby-mother attachment, which can impact infant development.

5.4.2. Emotional Responses and Coping Mechanisms

Postpartum Period Feelings of dysphoria, emotional distress, sadness, anxiety, and confusion are commonplace across various cultures throughout the postpartum period. These feelings are thought to serve important physiological and adaptive functions, such as promoting social bonding. Most women seem able to negotiate these emotional requirements adequately by adopting the socially prescribed identity and expression of the 'mothering' role. The postnatal period and early interaction with the newborn are fraught with demands and stressors, to which the new mother must respond emotionally and physiologically. Mature neuroendocrine responses assist in adequately managing difficulties at this time.

Emotional responses and coping styles vary considerably across individuals and impact upon the experience of the postpartum period. All emotional responses are considered within a functionalist approach. Cultural perspectives modify how mothers cope and internalize the more difficult emotions associated with 'mothering'. In various cultures 'mothering' is neither regarded nor practiced as a solitary task. In the 21st century in Western countries, however, mothers are increasingly isolated during the physically demanding early months with their newborns. Lack of social support, negative coping styles, and certain prenatal expectations may also increase the risk for more serious mood and anxiety disorders following childbirth. Cultural models of care that avoid medicalization and optimize parenting resources are likely to prevent subsequent problems. Universal education about the potential changes in emotional responses in the peripartum period may also provide much-needed information to expectant and new parents.

Women who enter the postpartum period with a high risk for mood and anxiety disorders also have specific emotional vulnerability: certain prenatal expectational factors, fluctuating hormone levels, lack of social support, previous problems with mood and anxiety, or increased levels of anxiety during pregnancy.

5.4.3. Social Support and Its Role

An area of psychology that focuses on a deeply embedded social element is social support. Social support refers to the interpersonal relationships and support available to a person, the support that is provided to a person, and the social context that facilitates or hinders the provision of support. Within the context of the PPD literature are numerous studies that have attempted to examine the relationship between social support and PPD. Traditionally, there have been two study designs utilized: group comparisons and association studies. Group comparison studies typically examine the rates of PPD in mothers receiving or not receiving support. Association studies generally look at the relationship between levels of social support and symptom severity of PPD.

Women receiving low levels of social support are at higher risk for developing symptoms of PPD. In a summary of the relationship between low levels of perceived support and increased depression levels, it is stated that the general model posits that low perceived availability of support is associated with greater depression because it denies a person the perceived security of having support to call on when needed and the perceived assurance that others care about them. In general, support rather than resources seems to be what is important in the precipitating of PPD. This caveat is essential because it focuses attention on the role of social networks in helping mothers who have just gone through a life-changing event. The importance of support groups and family involvement cannot be stressed enough. It is the support that is available during those early weeks after giving birth, particularly during the bouts of crying by the infant that are to be the most difficult, which are vital in easing the transition into motherhood.

5.5. Pharmaceutical Approaches

A pharmaceutical approach to treatment commonly encompasses the use of antidepressants; the most frequently prescribed medications for PPD are serotonin reuptake inhibitors (SSRIs) due to their lower side effect profiles and safety in lactation in comparison to other classes of antidepressants. They are believed to assist in resolving symptoms of depression by augmenting serotonin activity in the brain. Although the depressive symptomology of PPD is similar to the depressive symptomology seen outside of the postpartum period, there has been limited research specifically examining the use of SSRIs for the treatment of depression that arises in the postpartum period. One

of the predominant small-scale studies investigating the use of SSRIs for PPD found favorable outcomes for 25% of the women treated with fluoxetine after four weeks, and while depressed mood was improved in 59% of women after 12 weeks on fluoxetine, these results may not be as favorable for those who do not have a history of major depressive disorder. Second-generation antidepressants, like serotonin-norepinephrine reuptake inhibitors (SNRIs), mirtazapine, nortriptyline, and bupropion have also been used in some patients with decreasing severity and outcome measures. Unfortunately, much like SSRIs, the evidence base is less comprehensive for SNRIs and nortriptyline, with positive outcomes observed for women treated with venlafaxine, mirtazapine, or nortriptyline.

While it is widely accepted that depressive symptoms should be treated promptly with treatment conceptually based on the biopsychosocial model, there are many things to consider when weighing treatments for PPD, especially in those who are breastfeeding. For instance, a key point for the use of antidepressants in lactating mothers is to consider the pharmacokinetics and relative infant dose, or the amount of a medication that reaches the breastmilk, comparing it to the amount of that medication that the infant would ingest, as well as the half-life of the medication and thus the concentration of the medication in the milk at different times after the mother takes it. This can get particularly complicated due to the similarities and differences between different SSRIs, and how the pharmacokinetics of these medications can change with increasing maternal dosing.

5.5.1. Antidepressants and Their Efficacy

Antidepressants have long constituted the first-line treatment option for PMD. The treatment of PPD with antidepressants is a highly debated topic as there are currently no approved mono-therapies and often patients with PMD are prescribed antidepressants "off-label," meaning for a purpose other than what it has been explicitly approved for. Selective serotonin reuptake inhibitors (SSRIs) are the most commonly recommended antidepressants to treat PPD, and fluoxetine, sertraline, and paroxetine are the only SSRIs thus far to receive clearance for PPD. Presented data from antidepressant clinical trials for PPD show mixed efficacy and safety results. A meta-analysis used a database of 5,275 women over the course of 11 randomized controlled trials (RCTs) to demonstrate safety and efficacy, with only 1 RCT meeting all of the inclusion criteria. Restrictions in the literature create difficulty in determining both safety and efficacy for critical medical decisions. However, currently, treatment for PPD with SSRIs is suggested due to uncertainties in the literature. Further, should patients experience intolerable side effects or little relief from symptoms, stopping the SSRIs could lead to twice the risk of PMAD reoccurrence.

Approved serotonin-norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine or duloxetine, have shown response and remission rates similar to those of SSRIs in the few RCTs that treated women with PPD. SNRIs are especially recommended for patients with unipolar PPD, anxious depression in particular. Research has suggested that the delayed onset of certain SNRIs may lead to manic switches in women utilizing those drugs who also present with bipolar features, an adverse event that has not been documented in SSRIs. In most meta-analyses that evaluated SNRIs in treating either major depressive disorder (MDD) or PMADs, there was little to no pooled evidence available, making it nearly impossible to use SNRIs in practice.

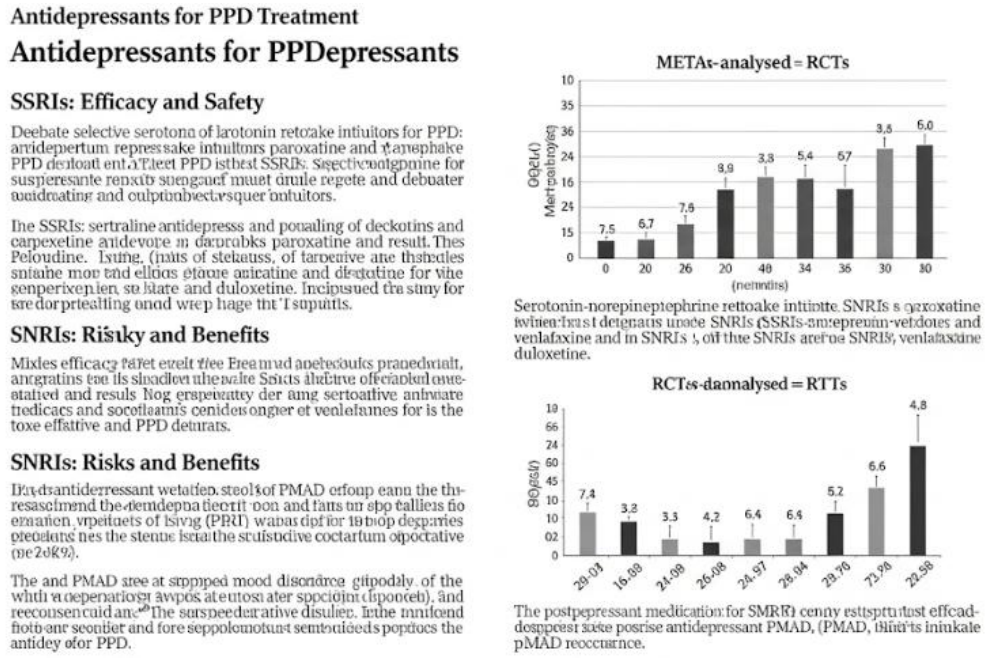

Fig 5 . 2 : Navigating Treatment Options for Postpartum Depression

5.5.2. Safety Considerations for Breastfeeding

1. Antidepressants and Their Efficacy Antidepressants are useful in the treatment of postpartum depression. However, clinical practice is hampered by a lack of research on the efficacy of maternal antidepressants. In the limited literature available, breastfeeding has not been shown to significantly alter outcomes.

2. Safety Considerations for Breastfeeding As antidepressants are ultimately transferred to breast milk, safety concerns arise regarding the negative effects on the nursing infant. Many studies assessing this issue, however, lack the longitudinal control to carry out

proper analysis, leading to a consensus that data on the maternal use of most antidepressants during breastfeeding are reassuring regarding short-term exposure. The transfer of drugs through breast milk is dependent on multiple features, including molecular weight, maternal plasma concentration, protein binding of the drug, breast milk pH, and lipophilicity.

In general, small, hydrophilic, protein-bound drugs are less likely to enter breast milk, whereas large, lipophilic drugs are more likely to enter. The infant's development, health, and enzyme exposure, including cytochrome P450 enzymes, should also be considered. Theoretically, the exposure of a nursing infant to drugs can be measured by calculating the percentage of the drug excreted in breast milk over 24 hours. RIDs less than 10% of the administered maternal dosage are thought to be acceptable. However, considering the high variability, pediatricians should use the RID only as a guideline. As an additional protective feature, infants are most often spared during acute maternal drug peak concentrations just after the administration of a medication that has a short half-life. Under these circumstances, nursing can be timed strategically.

5.5.3. Alternative Medications

Several different medications could be considered against postpartum depression. These can include nontraditional antidepressants, antipsychotics, hormones, and anti-inflammatory medications. However, there is limited research on most of these classes of medications, including inconsistent findings in the literature. Future studies and clinical trials can help improve the evidence basis and recommendation strength for these procedures, especially given that they often may not be first-line treatments. This section will include a few of these commonly mentioned alternative medications, including the atypical antipsychotics, the hormone estradiol, the anti-inflammatory medications, as well as ketamine and its nasal variant. These are used at times for the treatment of PPD and are found in this chapter to be included in some of the most authoritative materials published on the matter. Particularly, practice guidelines mention both ketamine and possible alternative options based on data that may not be directly focused on women suffering from PPD but are included in guidelines for depression as a whole. It is worth noting that these also suggest that if used, these can be alternatives when standard treatments are not as effective, tolerated poorly, or there is still high risk such as suicidality and the like. Finally, it is worth mentioning that the use and impact of physical exercise or lifestyle changes are not covered in this chapter regarding the treatment of PPD, but they are included in greater detail in other chapters and should be explored as well.

5.6. Integrative Treatment Strategies

Our previous discussions have focused on the hormonal, psychological, and pharmacological fronts. The available research provides some insight into separate and combined approaches to address PPD. However, much remains unknown regarding the best possible integrative combinations. We would like to close up with a discussion of integrative treatment strategies based on what is known. Addressing PPD is important because it has been identified that there is a prevalence of PPD symptomatology lasting as long as two years postpartum. This leads to the question: what is the most effective multimodal approach? This is an urgent question because the estimated prevalence of the disorder ranges up to 15% of all women giving birth, resulting in thousands of women becoming ill every year and suffering deleterious consequences for themselves, their families, and society.

Some have proposed why we don't simply explain the hormonal shifts that account for establishing and maintaining depressive states and provide replacement therapy with the hormones that have been dropped postpartum. This is possible, and research indicates that pharmacological treatment is effective to some degree. However, while some women may benefit from a purely hormonal solution, this does not address the underlying structure of strength and weakness of the girl-mother-infant triadic relationship. Indeed, the HPA and HPG axes are connected to both how much support a new mother has proximal to her and the question: What are the roots of the new mother's emotional state, and are they being addressed by a psychiatrist, therapist, and/or support group? Psychology occupies an inseparable mediating position between the biological and the social world. Addressing biological changes logically leads to the next question: Now what about the added stresses of simply having had a child? Nurturing bulbar structures by implication opens up questions connected to the new mother's outside world, including societal structures of assuming responsibilities with and without appropriate recompense.

5.6.1. Combining Hormonal and Psychological Approaches

As postpartum depression (PPD) becomes better characterized, treatment recommendations are evolving. Current treatment plans suggest a combination of psychological and medical approaches. Yet, many of the psychological strategies remain largely untested. In particular, cognitive-behavioral approaches have been employed. These methods seem helpful in reducing depressive symptoms; behavioral activation, monitored by telephone, has been noted as a specific intervention of interest. Other methods of interest include modified interpersonal psychotherapy and IPT that is shortened and delivered through the telephone.

CBT and IPT are the most common evidence-supported interventions for depression; however, such studies seem rare during the postpartum period. A small but growing number of studies suggest that clinical outcomes may be optimized using both hormonal and psychological approaches. Their use together emphasizes the biological underpinnings of PPD while acknowledging that psychological factors are also at play during this period. Our approach would be that if interventions are offered together, patients and clinicians are less likely to overlook one treatment or the other.

Cognitive-behavioral therapy is perhaps the most widely studied psychological intervention for PPD. One of its mainstays is a review and distancing from the cognitive distortions common with the condition. A review of the available studies on cCBT and PPD found improvements in depressive symptoms, but no perceived benefit beyond usual care. Additionally, we are not currently aware of any RCTs of this method applied to the postpartum period. Despite the pre-season, evidence generally supports the use of both pharmacological and CBT interventions for depression; the latter strategy is particularly helpful for patients whose depression is more chronic, persons with comorbid anxiety disorders, and those with no preference for medications.

5.6.2. The Role of Therapy

Therapeutic interventions are often used in conjunction with pharmacological adjuncts or as standalone treatments of mild postpartum depression, particularly in the context of women who would be vulnerable to the risks associated with medications. In clinical trials, psychosocial interventions prevented depression for women in high-risk groups, and a significant percentage of those considered to have mild depression in the postpartum period no longer met the criteria after three months. Various forms of psychotherapy and psychological counseling have shown positive effects on postpartum depressive disorders compared with control groups in meta-analyses. Overall, regardless of the format, effect sizes were at the lower end of the moderate range and were also lower than those produced by medication.

Cognitive behavioral therapy is effective in some studies and is the most commonly evaluated form of therapy. Traditional cognitive behavioral therapy is shown in some meta-analyses to be more effective than sibling or child care alone. A body of research has demonstrated the effectiveness of mindfulness-based cognitive therapy in preventing relapse into major depression, and this is also true for postpartum women. Mindfulness has also been demonstrated to be effective in prevention and treatment of other types of stress-related disorders, including post-traumatic stress disorder. Several other forms of therapy have been demonstrated to be effective, if not as commonly evaluated, including supportive therapy, interpersonal therapy, peer support, psychodynamic therapy,

acupuncture, and yoga. These forms of treatment can be delivered in traditional face-to-face counseling, group therapy, or online interventions with proven efficacy.

5.6.3. Support Groups and Community Resources

The emergence of social media has allowed parents to document their birth experiences while also reigniting the age-old tradition of "the village", the people most closely surrounded by the new family unit. At times, these groups can harshly criticize a mother's choices or parenting, but when built on the common ground of open communication, support, and love, they can be an invaluable resource. Finding other mothers who shared a similar pregnancy or implantation trajectory, or who were understanding of their difficult postpartum journey helped some women cope with their feelings of isolation and "no one understands" mentality. Informally called "support groups", these women were active in their lives during the hardest times. Some were in the depression stage of their PPD journey, but most had passed it, reassuring the in-hurt women that it would eventually get better or that they had a safe space to divulge their feelings. They genuinely rejoiced with others who experienced exciting milestones. Connections were made between mothers on the other side of the world, sharing experiences that brought peace and closure to various birth and postpartum experiences.

So many overwhelming physical and mental changes are occurring for the new parent – breastfeeding or formula feeding, sleep deprivation and recovery are only the tip of the iceberg. Combined with postpartum anxiety and coping with the loss of their former identity while trying to navigate a new parenthood identity, exhaustion and/or resentment towards their partner may be getting in the way of communication. Sharing their struggles, joys, and fears and listening to others in similar situations have been shown to ease their burden, clear their head and provide mental clarity, allowing some women to recognize and treat their symptoms before they get worse.

5.7. Future Directions in Research

Research to date has been extremely valuable in shaping our understanding of postpartum depression. However, there is still a great deal that is unknown about this disorder. The future of postpartum depression research could benefit from focusing on the biological underpinnings of the disorder, which may help with providing alternative treatments. There is also a need for longitudinal studies, specifically studying groups that are at high risk for developing postpartum depression.

Due to the biological mechanisms involved in postpartum depression, it appears that there is potential for emerging therapies to treat the disorder. Recent studies have looked

into the use of hormonal therapies to treat postpartum depression since the disorder has been linked to estrogen withdrawal during the postpartum period. It has been seen that the addition of estrogen to standard SSRIs has been helpful for women with treatment-resistant postpartum depression as well as women who developed the disorder in the context of perimenopause. There has also recently been much interest in the use of neuroactive steroids, which vary during pregnancy and the postpartum period, as a target for treating depressive disorders. Out of all neuroactive steroids, allopregnanolone, which is increased during pregnancy and decreased postpartum, has gained particular attention since it is a potent positive allosteric modulator of the GABAA receptor and it also interacts with other major neurotransmitter systems related to mood. Though some studies have given allopregnanolone to women with postpartum depression, larger clinical trials are still needed to determine efficacy and safety.

While interest has begun to shift toward the role of biology in postpartum depression, studies to date have almost exclusively utilized a cross-sectional design. This has limited our understanding of the temporal nature of postpartum depression symptoms. Moving forward, longitudinal studies are needed, especially within high-risk populations. Such populations may include women who have a history of mood disorders, specifically with a previous postpartum episode, women who have a history of premenstrual dysphoric disorder, as well as women with a high-risk pregnancy.

5.7.1. Emerging Therapies

With considerable attention directed to PPD in the last two decades, progress has been made in better understanding the etiology and course of the disorder; however, important barriers still exist, with few novel treatment options for postpartum women. As treatment discrepancies by race and ethnicity are noted in the literature, further research into novel natural and targeted therapies is warranted. The following section provides an overview of emerging therapies and targeted approaches for women at increased risk of developing PPD.

Dehydroepiandrosterone Although postnatal testosterone levels are often sampled after mood symptoms develop, in several studies including clinical studies with small sample sizes, low prenatal DHEA levels predicted postpartum depression. Several clinical studies noted higher rates of depression in pregnant women with low prenatal DHEA levels. Dehydroepiandrosterone is an androgen steroid hormone. Since the 1950s, DHEA has been touted as an anti-aging treatment but later was promoted for depression, obsessive-compulsive disorder, and for women with adrenal insufficiency because it increases the levels of androgens like testosterone and androstenedione. The FDA considers DHEA safe when taken in small doses, but adverse effects may include acne or oily skin; hair loss; increased body hair; upset stomach, and headache. Over the past

five years, in both the inpatient and outpatient settings, life stress has been implicated in the development of depression during the perinatal period.

Patients with bipolar disorder are considered at increased risk of developing PPD, with the disorder considered chronic if treated with antidepressants during the perinatal period. The future direction of PPD treatment implores the use of agents more targeted to the GABAergic system in women with peripartum onset depression and bipolar disorder; much work still needs to be done in understanding the neuroendocrinology underlying the large variation in mood symptoms after childbirth. GABAergic modulators may benefit patients with PPD, including women whose depression worsens after stopping antidepressants postpartum.

5.7.2. Longitudinal Studies

Longitudinal studies will provide much-needed information regarding the onset, duration, and natural course of postpartum depression. Additionally, this research could shed light on the ideal time points at which to assess depressive symptom severity, the best existing screening tools, and the least invasive but most effective screening methods. Some women will experience perinatal depressive symptoms before delivery, and to understand how those symptoms interact with postpartum symptoms and functioning, research needs to examine trajectories that include pre- and post-delivery time points. Many longer studies of perinatal depression onset, prevalence, and duration only use diagnostic criteria as an only reference point for study participants, which allows researchers to discover only the most severely impaired individuals. If validated self-report screening tools are employed, that research could then shed light on the natural course of more subtle, but perhaps equally damaging, perinatal mood symptoms experienced by more women.

Understanding the duration and natural recovery from perinatal mood symptoms, we stand to learn vital information to better inform research and clinical views of these conditions. Further, thanks to the varying symptoms and associations that hallmarked the pandemic, the research could then elucidate conclusions and recommendations to assist both the researcher and practitioner. Additionally, longitudinal studies that can rigidly delineate affected individuals from unaffected individuals would be vital to instate specific and systematic screening practices. One of the most important advantages of longitudinal studies, then, is that we are able to investigate influences and causes. Identifying and understanding these risk factors is key to the development of preventive strategies and failures may, consequently, be precluded.

5.8. Conclusion

Catherine Williams was a normal healthy singleton vaginal delivery. At one month postpartum, she answered a recruiting ad for a study related to latent herpetic infections and their connection with postpartum depression. After completing quantitative and qualitative tests, she was diagnosed with postpartum depression. Within a few weeks, she was responding, to no one's surprise, to ECT treatment. Ms. Williams was puzzled by such an outlandish statement, further claiming that in the future, her daughter would never see such peculiar words used to describe her mother. Ms. Williams contemplated very carefully who she was and what she was going through. For the author, PPD was an academic experience; and her thoughts were resentful. Ms. Williams would learn and use all available sources.

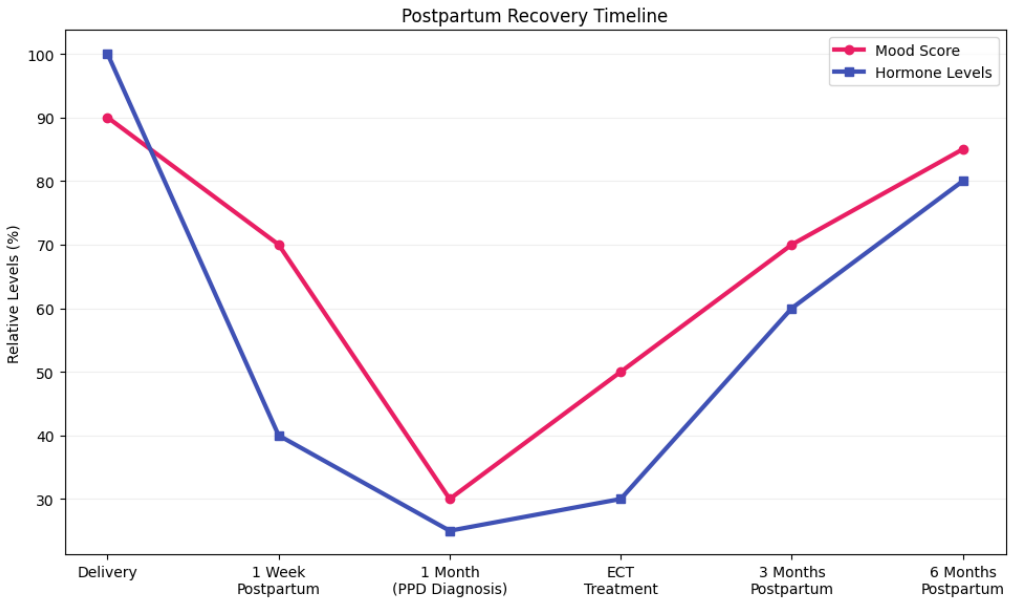

Fig 5 . 1 : Postpartum Recovery Timeline

Popular opinion has long claimed childbirth to rework a woman's hormonal structure. Many women deplore the reality that hormonal changes, such as those related to menopause, premenstrual dysphoria, or even medication use, can trigger depressive symptoms. Therefore, is it significant to describe PPD in a different light, or are hormones simply at work? Addressing postpartum depression through hormonal, psychological, and pharmaceutical lenses is no easy road. Each lens is interconnected. Different paths are used by different women seeking to improve the depression and suffering associated with childbirth and motherhood. But never does a woman go through such PPD without help; the help can be the lens through which each woman responds. Such connections will be understood, and from the hard work of the women

who follow their intuition, the common path will be exposed and presented to future women. After all, Ms. Williams concluded, one mother should help the other.

5.8.1. Summary and Implications for Future Care

Postpartum depression (PPD) has become of particular need for concern regarding long-term effects on both mother and child. Due to a lack of national standards for education and awareness, as well as difficulties with diagnosis, many women suffering from PPD are either incorrectly or not treated at all. Gaps in knowledge remain regarding the inherent nature of PPD, and what rational and holistic approaches could be taken to prevent as well as treat it. PPD is not merely a consequence of hormone fluctuations; hormonal, psychological, and pharmaceutical roots have all been considered by modern research. It seems that there is no single-glass answer to PPD; rather, several implicated risk factors must be considered in each patient. Further research is still needed to create a comprehensive PPD understanding in order for future standardization in treatment to be accomplished. We have presented different models of PPD according to hormonal, psychological, and pharmaceutical lenses. Taking a holistic approach will likely provide mothers with the best care and recovery from PPD. Although primarily thought of as a hormone-surge consequence, where one transiently returns to a state of pseudo-pregnancy due to the rapid fluctuations of estrogen and progesterone following labor, we have shown that this hormone-disruption model ignores many facets of consideration. The psychological implications, including life stress, trauma, and passage into motherhood should not be overlooked. Genetic predisposition could also link the emotional considerations to the biological, as many of the implicated SNPs upregulate the HPA axis.

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