Obsessive–Compulsive Disorders

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5.1 Obsessive–Compulsive Disorder

5.1.1 Definition and Epidemiology

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), defines obsessive–compulsive disorder (OCD) as the presence of obsessions, compulsions, or both, which must be time-consuming (e.g., more than 1 h per day) and cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. Obsessions are repetitive and persistent thoughts, images, or urges that are intrusive and unwanted and cause marked distress or anxiety. Compulsions are repetitive behaviors or mental acts that the individual feels driven to perform in order to reduce the distress and anxiety triggered by obsessions (Fig. 5.1) [1]. Common sets of obsessions and compulsions in patients with OCD include concerns about contamination together with washing or cleaning compulsions, fears of harm to oneself or others and related checking compulsions, forbidden or taboo thoughts such as intrusive aggressive, religious, or sexual thoughts together with mental rituals, and, finally, symmetry concerns and related repeating, ordering, or counting compulsions (Table 5.1) [2]. Preoccupations and rituals must be excessive or persisting, which distinguish the disorder from the occasional intrusive thoughts or repetitive behaviors, which are common in general population (e.g., double-checking that a door is locked).

The 12-month prevalence of OCD is from 1.1% to 1.8% of the population worldwide. Females are affected at a slightly higher rate than males in adulthood, although males are more commonly affected in childhood [1].

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M. Percudani et al. (eds.), *Key Topics in Perinatal Mental Health*,
https://doi.org/10.1007/978-3-030-91832-3_5

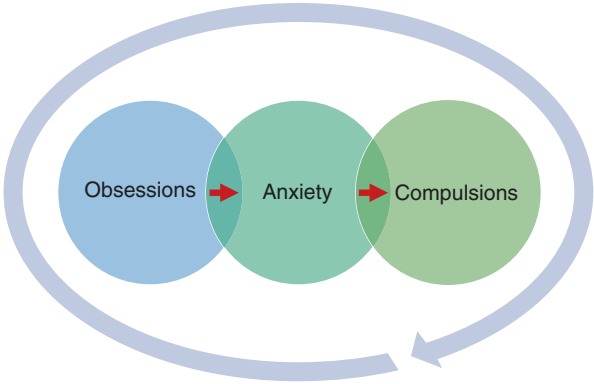

Fig. 5.1 The theoretical basis of obsessive–compulsive behavior

Table 5.1 Common obsessions and compulsions

Obsessions	Compulsions
Contamination concerns	Washing or cleaning rituals
Concerns about harm	Repetitive checking
Intrusive aggressive, sexual, or religious thoughts	Mental rituals or excessive praying
Symmetry concerns	Ordering, repeating, or counting rituals

5.1.2 Etiology

OCD is a complex psychiatric disorder with a multifaceted etiology. Experts propose a multifactorial model of inheritance where multiple genetic and biological risk factors act together with environmental stressors causing the disease onset. Several genome-wide linkage studies indicate that OCD is a polygenic disorder with many identified risk loci of small to moderate effect, including genetic variants within pathways for serotonin, dopamine, and glutamate or involved in immune and white matter pathways [3]. Biological factors (e.g., infection, altered concentrations of neurotrophic factors, pregnancy, and/or delivery) have also been suggested in OCD etiopathogenesis [3, 4]. Multiple evidence shows that exposure to pregnancy or to delivery increases the risk for OCD, with either pregnancy and delivery reported to be precipitants in 12.5% up to 40.0% of female OCD patients [5]. During pregnancy and the postpartum period, the disorder may be due to changes in the patient's natural body chemistry, including changes in hormonal levels (specifically progesterone and estrogen), or in functions of the brain [6, 7]. Besides biological causes, several environmental factors, such as experience of stressful life events (defined as a combination of major life events and subjective perception of the relevance of these events by the individual), contribute toward vulnerability to OCD [8, 9]. The most common stressful life events are emotional, financial, or health problems in the family, adverse perinatal events, starting or ending a significant relationship, moving to another city, and the death of a relative

or a friend [10]. Genetic and biological factors could be more determining in causing OCD in males. Conversely, environmental stressors, specifically adverse perinatal events and stressful or traumatic events, play a more important role in female patients [11].

5.1.3 Clinical Course

The average age at onset of OCD is 21 years, with medium onset age varying by gender (19 years for men, 22 for women) [12]. However, clinicians should investigate the age at onset of symptoms and the age when a diagnosis of OCD has been determined because these data can help predict the prognosis. This difference reflects the fact that generally OCD symptoms may appear early but the disorder may be diagnosed later when symptoms start causing clinically significant distress or impairment in social, occupational, or other important areas of functioning. The presence of significant differences in clinical profile depending on age at symptoms and disorder onset is tested; patients with early and intermediate age at symptoms onset are more likely to have an insidious mode of onset of OCD, compared to subjects with late age at symptoms onset. Furthermore, early age at disorder onset is associated with higher severity of symptoms on all OCD dimensions and with a greater disability [13]. Late-onset OCD, instead, is more likely to occur in females with long periods of subclinical obsessive–compulsive symptoms and usually shows a chronic clinical course [14].

Although OCD is generally thought to be a chronic disorder with persistent symptoms, increasing evidence shows that a subtype of OCD characterized by an episodic course may exist [15]. A chronic course implies a persistent presence of symptoms with phasic exacerbations and incomplete remissions, with significant distress and functional impairment. In the episodic course, symptoms are present only during an episode and, for the remaining time, symptoms remit for an interval of at least a month in a year, with or without treatment [16]. Some studies report differences between episodic and chronic OCD regarding sociodemographic and clinical characteristics: episodic OCD shows female preponderance, later age at onset, higher severity of obsessions and compulsions, and higher comorbidity of bipolar disorder [17].

Comorbidity is almost always present in OCD patients. With regard to general medical conditions, studies reveal high co-occurrence of OCD and physical diseases (particularly metabolic diseases): this association can be explained by the use of psychopharmacological treatments (such as second-generation antipsychotics) and the patients' severe self-neglect with the inability to perform basic activities of self-care and hygiene [18]. Concerning the association between OCD and other psychiatric diseases, recent studies confirm the higher prevalence of comorbid mood disorders, both depressive and bipolar disorders, with reciprocal influences on course and prognosis [19], but also anxiety disorders, substance use disorders,

and personality disorders, as compared to the general population [20–22]. In addition, OCD patients show a high risk of suicidality when compared to healthy controls [23]. At least one OCD patient out of ten attempts suicide during his/her lifetime, while nearly half of individuals with OCD have suicidal ideation. The most important predictors of suicidality in OCD patients are the severity of obsessions, presence of comorbid disorders (in particular substance use disorder, major depressive disorder, and personality disorder), and family history of completed suicide [24].

5.2 Obsessive–Compulsive Disorder in the Peripartum Period

Reproductive cycle events play an important role in the onset or exacerbation of OCD symptoms. Specifically, pregnancy, childbirth, and the postpartum period are clearly major life events that have been associated with an increased vulnerability for the development of OCD: an increasing number of studies show that pregnancy and postpartum may precipitate or exacerbate OCD in some women; moreover, it has been suggested that not only the perinatal period is a time of increased risk for the development of OCD, but also peripartum OCD presents distinct clinical features [25–27]. The prevalence of having at least one anxiety disorder during pregnancy or the postpartum period is estimated to be 20.7%, with a trend toward a greater prevalence in pregnancy versus the postpartum period [28]. Instead, the prevalence of OCD during pregnancy can vary depending on the gestational period. During the third trimester, a slightly higher value (3.5%) was found compared to the general population (2–3%). However, in the first and second trimesters, the prevalence of OCD is 0 and 0.5%, respectively [29]. In the postpartum period, the OCD prevalence varies from 2.4% to 11% [30]. Regarding women with preexisting OCD, 17% show worsening of symptoms during pregnancy as well as in the postpartum period [31]. Women with peripartum OCD are more likely to experience premenstrual worsening of OCD, compared to women with onset of the disease outside of the peripartum period. This suggests that some women with OCD may be differentially sensitive to reproductive cycle events. In spite of the effect of pregnancy and the postpartum period on the course of the disorder, there appears to be a lack of awareness about the common occurrence of OCD in this population.

5.2.1 Etiology

The etiopathogenesis of perinatal OCD has not been fully established. Because of the heterogeneous nature of the disease, many experts believe that perinatal OCD may be ascribed to a variety of etiologic processes and their interactions. These

include genetic, environmental, immunological, and hormonal factors. The dynamic nature of the hormonal environment has led to specific hypotheses regarding the effects of hormonal changes on peripartum OCD. Sex hormones play important roles in the central nervous system. Adrenal and gonadal steroids interact with neurotransmitters in an extremely complex balance. Steroid hormones can modulate neuronal transmission by a variety of mechanisms: they may affect the synthesis and/or release of neurotransmitters, as well as expression of receptors, membrane plasticity, and permeability [32]. Levels of estrogen, progesterone, and oxytocin vary significantly during the perinatal period. Cyclic fluctuations of gonadal hormones are not necessarily abnormal by themselves but may drive a vulnerability to OCD symptoms in some women. In fact, it is more likely to be that not all women with OCD have a vulnerability to hormonally triggered onset or exacerbation of symptoms, but instead represent a subset of them [33]. Specifically, there is growing evidence that suggest that onset or worsening of OCD symptoms during the perinatal period may be related to oxytocin fluctuations. Physiologically, oxytocin is involved in uterine contraction and lactation and in the initiation of maternal behavior; for this reason, levels of this hormone are elevated during the third trimester of pregnancy and the early postpartum period. In some recent studies, moreover, oxytocin has been reported to be more elevated in patients with OCD, compared with age and sex-matched control subjects [34]. Further work is needed in this area to be able to draw any definitive conclusions, but the potential role of oxytocin in the onset and exacerbation of OCD symptoms during the perinatal period should be considered [35]. Another area of exploration has been on fluctuations of estrogen and progesterone and their potential impacts on serotonergic transmission, which has been hypothesized to influence OCD symptoms. There has been speculation that the drop in estrogen and progesterone, which occurs after labor and delivery, may modulate the serotoninergic system, placing a subgroup of women with differential sensitivity to reproductive hormones at risk of OCD. The biological basis for this differential sensitivity remains unknown, but it has been speculated to represent the effect of genetic polymorphism in genes that regulate reproductive hormone signaling [36].

In addition to these biological processes, sleep disturbance, which is common among pregnant and postpartum women, may contribute to the development of OCD symptoms. Women's sleep is affected by pregnancy as early as the first trimester and, as pregnancy progresses, sleep quality worsens, with decreases in sleep duration and sleep efficiency. Following the birth, sleep quality continues to deteriorate, with worsened sleep efficiency and further sleep loss at night. The association between sleep disturbances and psychiatric disorders, including OCD, is recognized: circadian dysregulation causes alterations in cognitive, psychomotor, or emotional processing, which in turn could contribute to the onset of symptoms in a variety of psychiatric disorders [37]. Sleep deprivation is an important trigger for the first onset of peripartum OCD or worsening of previous OCD symptoms [38]. It is still unclear whether women

with sleep deprivation are at greater risk of developing postpartum OCD than women without sleep disturbance, but some studies speculate that neuroinflammation may be the mechanism by which sleep changes contribute to the onset or worsening of OCD [39, 40].

Furthermore, other risk factors for peripartum OCD include primiparity, personal history of depression, obsessive–compulsive and avoidant personality disorder, and family histories of mood disorders [41]. Finally, perinatal risk factors might also be associated with the subsequent development of OCD: cesarean section delivery, preterm birth, low birth weight, breech presentation, and low Apgar scores at 5 min after delivery are considered critical environmental risk factors for OCD onset or worsening of previous OCD [5].

5.2.2 Clinical Features and Course

OCD symptoms mostly occur during the third trimester of gestation and during the first 4 weeks after childbirth [7, 29]. Although the clinical presentation of peripartum OCD varies widely, obsessions are usually more frequent than compulsions [42]. Obsessions often include concerns about the well-being of the fetus or baby, and aggressive obsessions appear to be the most common: most women experience disturbing intrusive thoughts of harming fetus or newborns, accidently or intentionally (e.g., intrusive thoughts of shaking, dropping, throwing, stabbing, drowning, or suffocation babies). Secondary to obsessions, common compulsions include repetitive and ritualistic checking (e.g., repeatedly checking breathing or body of babies). Furthermore, avoidance behaviors regarding things that they fear could harm the baby are common (Table 5.2) [26, 43]. It is important to distinguish between postpartum OCD symptoms and postpartum psychosis, as both may involve ideas of harming newborns. Postpartum obsession thoughts are not associated with an increased risk of committing harm and are experienced as senseless, unwanted, and inconsistent with a person's typical personality or behavior. Conversely, postpartum psychosis typically includes psychotic symptoms, confusion, mood alteration, and agitation.

In addition to aggressive obsessions, women with pregnancy or postpartum OCD usually report contamination obsessions, with related checking and washing or cleaning compulsions, because of fear of microorganism contamination to the fetus or to the infant (Table 5.2) [36]. Perinatal OCD symptoms, especially when severe

Table 5.2 Common obsessions and compulsions in the peripartum period

Obsessions	Compulsions
Intrusive aggressive thoughts(e.g., intrusive thoughts of shaking, dropping, throwing, stabbing, drowning, or suffocation babies) *Contamination concerns*	*Repetitive checking* (e.g., repeatedly checking breathing or body of babies and avoidance of dangerous things) *Washing or cleaning rituals and repetitive checking*

or persistent, may cause severe personal distress, significant levels of anxiety, and feelings of guilt for having to spend large amounts of time dealing with obsessions and compulsions. Consequently, women may be less available to their children physically and emotionally [44]. However, the impact of peripartum OCD on the neurodevelopment of children is unknown. The disorder also affects the relationships, as family members may find it difficult to cope with the disorder for having to engage in compulsive rituals themselves or due to the need to provide constant reassurance [36, 45].

It is unclear whether OCD with pregnancy and postpartum onset is transient or persistent, but it is considered that OCD with peripartum onset tends to become chronic, especially when the disorder is not treated [41, 46].

5.2.3 Comorbidities

Psychiatric comorbidities are usually to be common in women affected by peripartum OCD. Approximately 27.5% of women have an anxiety disorder, and 70.6% have a mood disorder [45]. Between the first group of comorbidities, the most common comorbid diagnoses are generalized anxiety disorder and specific phobia [47]. Among mood disorders, major depression is the most common comorbid disorder in women with peripartum OCD, and it is associated with chronic course and poor prognosis [41, 48–50]. Furthermore, approximately 20% of women have a comorbid diagnosis of bipolar disorder [51]. Lastly, OCD with onset in the peripartum period shows higher comorbidity rates of personality disorders, specifically obsessive–compulsive, avoidant, and dependent [47].

5.2.4 Diagnosis

Symptoms of OCD should be differentiated from physiological thoughts in which women care about their children's safety, occurring in 34–65% of women after delivery [52]. These physiological thoughts of worry are usually temporary and do not interfere with normal daily functioning or childcare responsibilities. In contrast, obsessions and compulsions are clearly maladaptive and time consuming, causing distress and functional impairment [53]. Identification of peripartum OCD and its differentiation from the other common peripartum psychiatric disorders can be challenging for several reasons [54]. First, OCD symptoms may not be recognized by women as being pathological, or feelings of embarrassment and guilt may prevent women from communicating symptoms to their families or caregivers. Second, due to a general lack of awareness of peripartum OCD, clinicians may fail to elicit information about obsessions and compulsions. Due to their increased risk of developing OCD, women with prior histories of major depression, anxiety disorders, or OCD should be identified as soon as possible

during pregnancy and followed closely. Similarly, women with depression or anxiety disorders in the postpartum period should be screened for obsessive–compulsive symptoms [55]. The Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) is the most commonly used scale to evaluate the severity of symptoms and to monitor response to treatment. However, it has not been validated in women with postpartum OCD [56, 57]. The Perinatal Obsessive–Compulsive Scale (POCS) is the only one that was developed and validated in women with perinatal OCD [58]. POCS is a self-report questionnaire with a prenatal and a postpartum version. In this scale, each symptom is assessed on the severity and interference scales. The Edinburgh Postnatal Depression Scale and the State-Trait Anxiety Inventory can be used to identify and monitor contemporary symptoms of depression and anxiety, respectively [59, 60]. Moreover, women with comorbid depression should be further evaluated to determine whether depressive episodes are related to major depressive disorder or bipolar disorder.

5.2.5 Treatment

Usually, treatment of peripartum OCD can be carried out in outpatient settings. Inpatient settings may be indicated for women who are at risk for suicide, are unable to provide adequate self-care, and have a co-occurring psychiatric disorder that requires hospital treatment [61]. Most OCD treatment guidelines support the use of antidepressant drugs and cognitive behavioral approaches as first-line treatment [62–64]. The selection of treatment modality should depend on the nature and severity of OCD. In general, cognitive behavioral therapy is recommended for individuals with mild to moderate OCD and good insight into illness. Conversely, pharmacological treatment should be indicated in cases of moderate to severe OCD, comorbidity with major psychiatric disorder, risk of suicide, OCD-related sleep and eating disorders, and unresponsiveness to cognitive behavioral therapy [63–65]. Due to lack of controlled data and absence of studies on pharmacotherapy of peripartum OCD alone (i.e., without comorbid psychiatric disorders), no firm recommendations can be offered for drug treatment of peripartum OCD [66]. However, similar to treatment of OCD with onset outside peripartum period, selective serotonin reuptake inhibitors (SSRIs) are the first choice as pharmacological treatment for OCD, as abundant available data support their relative safety for embryo, fetus, and infant, while serotonin-norepinephrine reuptake inhibitors (SNRIs), clomipramine, and other antidepressants are recommended as a second- and third-line choice [67]. SSRI use in pregnancy seems to be associated with a small absolute risk of congenital heart defects and persistent pulmonary hypertension of newborns (PPHNs), as well as an absolute risk of transitory poor neonatal

adaptation syndrome but mostly of mild severity [68]. It is important to consider the risks and benefits of pharmacotherapy during pregnancy and the postpartum period. Risks to fetuses and newborns should be weighed against the potential harm of untreated obsessive and compulsive symptoms and co-occurring disorders. The choice of the right SSRI depends on individual characteristics of patients, such as nature and severity of OCD symptoms, prior treatment response, and comorbid conditions. Thus, no SSRI drug has to be avoided in particular [69]. In patients who had an inadequate response to SSRI therapy, antipsychotic treatments may be added [70, 71]. The amount of safety data regarding antipsychotic treatment, especially second-generation anti-psychotics (SGAs), during pregnancy is rapidly evolving. From a safety point of view, a substantial and reassuring amount of data overall do not suggest a clinically meaningful increased risk of congenital malformations. However, data on other pregnancy outcomes of interest (i.e., miscarriage, stillbirth, preterm birth, small for gestational age, neonatal adaption, and childhood neurodevelopment) are overall insufficient to provide confident estimates. It is imperative that clinicians consider individual disease history, clinical characteristics, treatment response, adverse reaction profile, and patient preferences, when choosing specific SGA treatment during pregnancy and peripartum period [72]. If medication is needed, monotherapy is recommended, especially at a minimum effective dose and in slow-release formulations twice or more times daily in order to minimize high peak concentrations [73]. Besides, physiological changes that occur during pregnancy induce pharmacokinetic changes (e.g., increased volume of distribution, modified cytochrome P450 activity, increased glomerular filtration rate) and may result in decreases in drug concentrations and effect [74]. Therefore, dose adjustments during pregnancy are required. Related to breastfeeding, most antidepressants are excreted in low concentrations in breast milk, and only a few reach levels considered unsafe for infants ($\geq$10% of the maternal weight-adjusted dose in breast milk). Available data do not support a formal limitation of SSRI use during breastfeeding [69, 75]. However, sertraline is one of the safest and most known medications to be used during breastfeeding, owing to its documented low levels of exposure in breastfed infants and to the very limited number of adverse events described in the literature [76].

In conclusion, based on current knowledge and due to the absence of consensus between treatment recommendations, a pragmatic-personalized risk–benefit analysis to propose pharmacological treatment before, during, and after pregnancy appears to be crucial in OCD patients [77, 78]. Personalized plans based on a shared decision-making process may help to reduce the stigma associated with the disorder, an improved pregnancy plan, and a higher awareness of risks.

Executive summary

Prevalence

- The prevalence of having at least one anxiety disorder during pregnancy or the postpartum period is estimated to be 20.7%
- The prevalence of OCD during pregnancy can vary depending on the gestational period. During the third trimester, a slightly higher value (3.5%) was found compared to the general population (2–3%). However, in the first and second trimesters, the prevalence of OCD is 0 and 0.5%, respectively. In the postpartum period, the OCD prevalence varies from 2.4% to 11%
- Also, 17% of women affected by preexisting OCD show worsening of symptoms during pregnancy and the postpartum period

Etiology

- Perinatal OCD may be ascribed to a variety of etiologic processes. These include genetic, environmental, immunological, and hormonal factors
- Cyclic fluctuations of gonadal hormones may drive a vulnerability to OCD symptoms in some women due to their potential interaction with serotonergic pathways. Moreover, the onset or worsening of OCD symptoms during the perinatal period may be related to physiological oxytocin fluctuations
- Sleep deprivation is an important trigger for the first onset or worsening of OCD. Some studies speculate that neuroinflammation may be the mechanism by which sleep disturbance contributes to OCD onset

Clinical features and course

- OCD symptoms mostly occur during the third trimester of gestation and during the first 4 weeks after childbirth
- Aggressive obsessions appear to be the most common during pregnancy and the postpartum period: Most women experience disturbing intrusive thoughts of harming fetuses or newborns. Secondary to these obsessions, common compulsions include repetitive and ritualistic checking
- Women with pregnancy or postpartum OCD usually report contamination obsessions, with related checking, washing, or cleaning compulsions
- It is unclear whether OCD with pregnancy and postpartum onset is transient or persistent, but it is considered that it tends to become chronic

Comorbidities

- Approximately 27.5% of women have an anxiety disorder, and 70.6% have a mood disorder, in particular generalized anxiety disorder, specific phobia, major depressive disorder, and bipolar disorder
- OCD with onset in the peripartum period shows higher comorbidity rates of personality disorders, specifically obsessive–compulsive, avoidant, and dependent

Diagnosis

- Due to their increased risk of developing OCD, women with prior histories of major depressive disorder, anxiety disorders, or OCD should be identified as soon as possible during pregnancy and the postpartum period
- The Yale–Brown obsessive–compulsive scale (Y-BOCS) is the most commonly used scale to evaluate the severity of symptoms and to monitor response to treatment, but it has not been validated in women with postpartum OCD
- The perinatal obsessive–compulsive scale (POCS) is the only scale that was developed and validated in women with perinatal OCD

Treatment

- Most OCD treatment guidelines support the use of antidepressant drugs and cognitive behavioral approaches as first-line treatment
- No firm recommendations can be offered for drug treatment of peripartum OCD. However, selective serotonin reuptake inhibitors (SSRIs) are the first choice due to their relative safety for the embryo, fetus, and infant
- Monotherapy is recommended at a minimum effective dose and in slow-release formulations twice or more times daily
- Most antidepressants are excreted in low concentrations in breast milk. However, available data do not support a formal limitation of SSRI use during breastfeeding

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