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Brazilian Psychiatric Association consensus for the management of psychiatric emergencies in pregnancy and postpartum period

Consenso da Associação Brasileira de Psiquiatria para o manejo das emergências psiquiátricas na gestação e puerpério

Consenso de la Asociación Brasileña de Psiquiatría para el manejo de emergencias psiquiátricas en el embarazo y puerperio

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ABSTRACT:
Introduction: Emergencies in the pregnancy and postpartum are less frequent than in other groups, but not uncommon. However, the literature on the subject is scarce and controversial. **Objective:** The objective of this article is to present some recommendations for the management of the most common psychiatric emergencies that may occur in pregnancy or postpartum period. **Method:** These procedures were focused on the discussion and integration of the findings from peer-reviewed published research on the topic. We searched electronic database PubMed. Relevant abstracts were identified using the following search terms: Psychotropics medications at pregnancy and breastfeeding: (((psychotropic medications) AND (pregnancy)) OR (psychotropic medications)) AND (breastfeeding) - Psychiatric emergencies: (((((((psychiatric emergencies) AND (pregnancy)) OR (psychiatric emergencies)) AND (postpartum)) OR (psychiatric emergencies)) AND (peripartum)) OR (psychiatric emergencies)) AND (breastfeeding). Inclusion criteria included papers

published (or in press) about pregnancy or breastfeeding or postpartum from December 2000 to January 2021 that focused on agitation in psychiatric emergencies. **Main Results:** We present recommendation for pharmacological treatment, psychomotor agitation, suicide behavior, psychotic disorders and mania, severe depression, and substance use disorders. **Conclusion:** Although many of the recommendations are empirical, it is already possible to rely on information that provides better results and safety for the patient and her infant.

Keywords: pregnancy, postpartum, psychiatric emergencies, mental disorder

RESUMO:

Introdução: Emergências na gravidez e no puerpério são menos frequentes do que em outros grupos, mas não incomuns. No entanto, a literatura sobre o assunto é escassa e controversa. **Objetivo:** O objetivo deste artigo é apresentar algumas recomendações para o manejo das emergências psiquiátricas mais comuns que podem ocorrer na gravidez ou no puerpério. **Método:** Esses procedimentos foram focados na discussão e integração dos achados de pesquisas publicadas e revisadas por pares sobre o tema. Pesquisamos bancos de dados eletrônicos usando PubMed. Resumos relevantes foram identificados usando os seguintes termos de busca: Psychotropics medications at pregnancy and breastfeeding: (((psychotropic medications) AND (pregnancy)) OR (psychotropic medications)) AND (breastfeeding) - Psychiatric emergencies: (((((((psychiatric emergencies) AND (pregnancy)) OR (psychiatric emergencies)) AND (postpartum)) OR (psychiatric emergencies)) AND (peripartum)) OR (psychiatric emergencies)) AND (breastfeeding). Os critérios de inclusão incluíram artigos publicados (ou no prelo) sobre gravidez ou amamentação ou pós-parto de dezembro de 2000 a janeiro de 2021 que enfocassem agitação em emergências psiquiátricas. **Principais resultados:** Apresentamos recomendação para tratamento farmacológico, agitação psicomotora, comportamento suicida, transtornos psicóticos e mania, depressão grave e transtornos por uso de substâncias. **Conclusão:** Embora muitas das recomendações sejam empíricas, já é possível contar com informações que proporcionam melhores resultados e segurança para a paciente e seu bebê.

Palavras-chave: gravidez, pós-parto, emergência psiquiátrica, desordem mental

RESUMEN:
Introducción: Las urgencias en el embarazo y puerperio son menos frecuentes que en otros grupos, pero no infrecuentes. Sin embargo, la literatura sobre el tema es escasa y controvertida. **Objetivo:** El objetivo de este artículo es presentar algunas recomendaciones para el manejo de las emergencias psiquiátricas más comunes que pueden presentarse en el embarazo o puerperio. **Método:** estos procedimientos se centraron en la discusión y la integración de los hallazgos de investigaciones publicadas revisadas por pares sobre el tema. Se realizaron búsquedas en base de datos electrónica PubMed. Los resúmenes pertinentes se identificaron mediante los siguientes términos de búsqueda: Psychotropics medications at pregnancy and breastfeeding: (((psychotropic medications) AND (pregnancy)) OR (psychotropic medications)) AND (breastfeeding) - Psychiatric emergencies: (((((((psychiatric emergencies) AND (pregnancy)) OR (psychiatric emergencies)) AND (postpartum)) OR (psychiatric emergencies)) AND (peripartum)) OR (psychiatric emergencies)) AND (breastfeeding). Los criterios de inclusión incluyeron artículos publicados (o en prensa) sobre el embarazo o la lactancia o el puerperio desde diciembre de 2000 hasta enero de 2021 que se centraron en la agitación en emergencias psiquiátricas. **Principales resultados:** Presentamos recomendación de tratamiento farmacológico, agitación psicomotora, conducta suicida, trastornos psicóticos y manía, depresión severa y trastornos por uso de sustancias. **Conclusión:** Aunque muchas de las recomendaciones son empíricas, ya es posible contar con información que brinda mejores resultados y seguridad para la paciente y su lactante.

Palabras clave: embarazo, puerperio, emergencia psiquiátrica, trastorno mental

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Introduction

Pregnancy and postpartum, far from being protective factors against psychiatric disorders, can aggravate pre-existing or trigger new psychiatric disorders. Approximately 1 in 13 women experience a new onset of a major depressive episode during pregnancy and 1 in 7 experience an episode in the peripartum [1, 2].

Among women with a pre-existing mood disorder, the rate of relapse in peripartum is 10 to 30% for unipolar depression [2, 3, 4] and 52% for bipolar depression or the recurrence of a manic episode [2, 5]. Similarly, prenatal and postnatal anxiety disorders (all anxiety subtypes) are diagnosed in 15.2% of women during pregnancy and 9.6% of women post-birth [2, 6].

During the first year after delivery, women with a psychiatric disorder are at the highest risk for psychiatric hospitalization [1, 7] and suicide is the leading cause of maternal death [2, 7]. Psychosis and suicidal ideation with onset during pregnancy and postpartum are psychiatric emergencies which require prompt intervention. It is worth remembering that cases of puerperal psychosis are uncommon, with an estimated prevalence of 0.2% among live births, however, these cases have the potential for serious outcomes such as infanticide and maternal suicide [3].

In emergency settings, clinicians must assess maternal and infant risk when determining individuals who are appropriate for outpatient management and those who require hospital admission.

Despite the importance and impact of psychiatric emergencies, evidence-based strategies for management of psychiatric emergencies in the perinatal period are limited. In the present review, we outline the management of the most common psychiatric emergencies in the peripartum period.

Methods

This work has been driven by a panel of global experts on severe mental health illnesses, selected by Brazilian Psychiatric Association. These procedures were focused on the discussion and integration of the findings from peer-reviewed published research on the topic, including reviews and meta-analysis, as well as clinical trial reports and the most relevant guidelines on agitation, with the aim to integrate them into an expert consensus.

Search strategy and selection criteria

We performed an extensive literature search within the different medical specialties who have published on this topic. We searched electronic database using PubMed. Relevant abstracts were identified using the following search terms: **Psychotropics medications at pregnancy and breastfeeding:** (((psychotropic medications) AND (pregnancy)) OR (psychotropic medications)) AND (breastfeeding) - **Psychiatric emergencies:** (((((((psychiatric emergencies) AND (pregnancy)) OR (psychiatric emergencies)) AND (postpartum)) OR (psychiatric emergencies)) AND (peripartum)) OR (psychiatric emergencies)) AND (breastfeeding). Inclusion criteria included papers published (or in press) about pregnancy or breastfeeding or postpartum from December 2000 to January 2021 that focused on agitation in psychiatric emergencies.

Topics:

Psychotropics medications at pregnancy and breastfeeding

(((psychotropic medications) AND (pregnancy)) OR (psychotropic medications)) AND (breastfeeding)
https://pubmed.ncbi.nlm.nih.gov/?term=%28%28%28psychotropic+medications%29+AND+%28pregnancy%29%29+OR+%28psychotropic+medications%29%29+AND+%28breastfeeding%29&filter=pubt.clinicaltrial&filter=pubt.guideline&filter=pubt.meta-analysis&filter=pubt.randomizedcontrolledtrial&filter=pubt.review&filter=pubt.systematicreview&filter=years.2001-2021

Psychiatric emergencies
(((((((psychiatric emergencies) AND (pregnancy)) OR (psychiatric emergencies)) AND (postpartum)) OR (psychiatric emergencies)) AND (peripartum)) OR (psychiatric emergencies)) AND (breastfeeding)
https://pubmed.ncbi.nlm.nih.gov/?term=%28%28%28%28%28%28%28psychiatric+emergencies%29+AND+%28pregnancy%29%29+OR+%28psychiatric+emergencies%29%29+AND+%28postpartum%29%29+OR+%28psychiatric+emergencies%29%29+AND+%28peripartum%29%29+OR+%28psychiatric+emergencies%29%29+AND+%28breastfeeding%29&filter=pubt.clinicaltrial&filter=pubt.guideline&filter=pubt.meta-analysis&filter=pubt.randomizedcontrolledtrial&filter=pubt.review&filter=pubt.systematicreview&filter=years.2001-2021

Main Results

Recommended environment for attending psychiatric emergencies during pregnancy and the postpartum period

Although there are several models of care for psychiatric emergencies, this group recommends that psychiatric emergencies in pregnancy and postpartum period be assessed to in the emergency room. And encompass physical, obstetric-gynecological, and psychiatric assessment in all cases. Main recommendations are presented at Table 1.

Pharmacological considerations

The FDA changed the categories of risk of pregnancy in the prescription and labeling of biological drugs in 2015 to make them more relevant to patients and health professionals.

Since there are lack of studies examining the safety of psychotropic agents during pregnancy and considering psychiatric emergencies life-threatening conditions that need to be correctly approached, three points should be considered:

1. Consider risks, whether the medication will be used for a short period, only during the emergency, or will be for continuous longer-term use.

2. Consider risks versus benefits. The consequences of severe non-treated mental illness often outweigh the risks (which are generally small) of using most psychotropic medications that are typically used in the pregnancy and postpartum period.

3. When choosing the drug, consider the period (gestational age, early or late postpartum), the ability of the drug to cross the placental barrier or

its concentration in the breast milk, along with the risk of severe adverse reactions based on current knowledge.

Antipsychotics

In psychiatric emergencies, antipsychotics are often indicated for psychomotor agitation linked to acute exacerbations of mental disorders, including psychotic disorders, mood disorders, and others. One study found that quetiapine, risperidone, haloperidol, and olanzapine cross the placental barrier with greater difficulty [8].

In another study, the rate of placental passage was higher for olanzapine, haloperidol, risperidone, and quetiapine [9]. There was a trend towards higher rates of low birth weight (30.8%) and admission to a neonatal intensive care unit (30.8%) among neonates exposed to olanzapine [9]. There was a trend toward higher rates of low birth weight (30.8%) and neonatal intensive care unit admission (30.8%) among neonates exposed to olanzapine [9]. Intrauterine signs of exposure seen in babies exposed to antipsychotics include restlessness, dystonia, hypertonia, and tremor. For manic symptoms, olanzapine, risperidone, quetiapine and haloperidol are considered effective and studies on the reproductive safety of such drugs have not identified a significant association with major congenital malformations [10].

In cases of psychotic manifestations associated with unipolar depression, quetiapine has some favorable characteristics: antidepressant properties; adjunct drug of choice in refractory depression; lower levels of placental passage compared to haloperidol, olanzapine and risperidone [11].

Among the most available first generation low-power antipsychotics, chlorpromazine has a favorable reproductive safety profile, with no significant association with major malformations. Another available phenothiazine, promethazine, recommended are considered safe using during pregnancy in some psychiatric emergency protocols [12].

During lactation, typical antipsychotics, such as haloperidol, were not linked to frequent or serious adverse effects in infants. Among the atypical antipsychotics, olanzapine and quetiapine stands out, due to recent studies that demonstrate generally low risk of serious adverse effects, as well as low concentration in breast milk [13, 14, 15]. Risperidone can be used for breastfeeding under medical supervision. On the other hand, clozapine and amisulpiride are contraindicated [14].

Mood stabilizers

Each pregnancy should be closely monitored and appropriate screening tests (e.g., fetal cardiac in the first trimester for patients that use lithium) should be performed [15].

Divalproex and carbamazepine should be avoided during pregnancy due to elevated risk of neural tube defects (up to 5%), even higher incidences of other congenital abnormalities, and evidence of delayed neurological development in children at 3 years of age and loss of an average of nine IQ points [15, 16]. There was no increase in the rates of birth defects with the use of lamotrigine alone [16, 17].

The risks and benefits of taking medications while breastfeeding should be discussed with the patient, as well as the need for continuous monitoring of babies is also fundamental [15].

The available data support the use of lithium as a possible option. Carbamazepine and valproic acid are also considered to be relatively safe, and lamotrigine can be used in low doses [14, 18].

Benzodiazepines

In psychiatric emergencies, benzodiazepines are especially indicated for acute anxious manifestations experienced by the patient, which are usually exacerbations of anxiety disorders or acute intoxication by stimulants or substance withdrawal syndrome by alcohol [19].

Research on the reproductive safety of benzodiazepines has produced controversial results. Most studies indicate absence of an association of congenital malformations with the use of benzodiazepines during pregnancy [20, 21].

Generally, (for all benzodiazepines) it is recommended that, if there is an indication for use in pregnant women, the lowest therapeutic dose should be used for the shortest possible period. During lactation, the sedative effects of benzodiazepines in children are generally mild or absent. It is importance in the context of medical emergencies is the apparent absence of risk during lactation when benzodiazepine is administered once daily, intermittently, or in the short term of up to 72 hours [22].

Antidepressants

Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressants for the treatment of depression, OCD, anxiety, and other disorders throughout pregnancy, as they are not significantly related with an increased risk for fetal malformations in women with psychiatric disorders [8, 23, 24].

Paroxetine was thought to be associated with an increased absolute risk of cardiac malformation of 0.5-1.0% more than the general population until a few years ago [25].

Fluoxetine was also associated with heart defects in the past, but newer studies have shown that after adjustment for depression associated confounders, such as health life style, addition, smoking, neither fluoxetine nor paroxetine appear to be associated with additional risk beyond baseline significant risk [26].

The association between the SSRIs antidepressant use and cardiac defects is attenuated when adjusting for these confounders and show no significance risk in most of recent studies [27]. After delivery, the most indicated drugs for treatment are SSRIs during breastfeeding, especially citalopram, escitalopram, and sertraline [8, 28-33].

Serotonin and norepinephrine reuptake inhibitors (SNRIs) and noradrenaline-dopamine re-uptake inhibitors (NDRIs). IRSNs may be options in pregnancy, including duloxetine and venlafaxine [8]. Although bupropion is not the first option for depression in pregnancy, it may be a choice for women who have not responded to other antidepressants [8].

Besides data observed bupropion active metabolites cross the placenta to the fetal circulation [34] some studies have found no association with major malformations [8]. In general, serotonin norepinephrine reuptake inhibitors (SNRIs) appear to have minimal passage into breastmilk, whereas bupropion is avoided if possible due to some case reports of infant seizure [35].

Finally, while tricyclic antidepressants are also not the first or second line of choice, they may be an option for women who have not responded to other medications. They have a modest risk of spontaneous abortion, premature birth, and low birth weight, but may be secondary to other factors, such as psychiatric illness itself [8].

Therapeutic drug monitoring allows monitoring of serum levels and appropriate dose adjustments during [36]. Tricyclic antidepressants have greater passage into breastmilk than SSRIs and so are avoided when possible, but if tricyclics are used, nortriptyline is considered to have the best safety profile; doxepin is considered contraindicated given case reports of adverse events in exposed infants [29].

Psychomotor agitation

Psychomotor agitation in the pregnancy and postpartum period usually occurs in the context of psychiatric disorders and may lead to loss of insight and/or judgment and self-determination; this is mainly seen in cases of psychotic syndromes, mania, and severe depression.

During the gestational period, this is particularly important because women in these conditions are at a higher risk for drug use and suicide attempts [37]. Furthermore, the postpartum is a stage of risk for worsening of some psychiatric conditions [38].

Management:

In an emergency room, the healthcare provider managing a situation of psychomotor agitation in pregnancy and postpartum period women should be informed about:

1. Ensure the safety of the patient, her offspring, other patients, and the medical staff [39-41]
2. Exclude organic causes. The clinician should discard cerebrovascular, metabolic, immunological, and drug´s related conditions. Therefore, a careful clinical history, including collateral information from family members is critical, in addition to requesting laboratory, imaging tests, and possible collaboration with other healthcare members may also be required in order to improve the quality of care from other specialties [40, 42, 43]. It is important that clinical history considers information that involves the particularities of pregnancy: previous pregnancies, previous types of delivery, and complications (including behavioral ones) of previous pregnancies. It is also important to include physical and neurological examination.
3. Consideration of Environment and use of verbal de-escalation techniques [44, 45]. It is important that the patient remain in an environment that is as peaceful as possible, with few visual and auditory stimuli and preferably with the companion of a supportive person.

4. Psychotropic drugs to handle with psychomotor agitation in the pregnancy and postpartum period should be prescribed with caution, in the lowest possible dose, and only in situations in which verbal de-escalation are not sufficiently effective [40]. All psychiatric drugs can cross the blood-brain barrier [9]. In pregnant women, the exposure to psychotropic drugs can potentially increase the likelihood of three types of risks: congenital malformations when used in the first 12 weeks, perinatal syndromes, such as intoxication or withdrawal symptoms, and late-onset neurobehavioral changes, such as delayed neuropsychomotor development and low intelligence quotient [46]. We recommend haloperidol in monotherapy or benzodiazepine in monotherapy. However, we advise you to avoid their combination, which should be reserved only if very necessary [40, 47]. The suggested medication options for severe agitation in the pregnancy and peripartum are listed in Table 2.
5. Physical restraint may be preferred to avoid harming the fetus or to avoid self-harm or harming the fetus [48, 49]. However, extreme caution must be exercised when performing physical restraint of pregnant women in the second or third trimester. The routinely used four-point contention (limbs) in supine position is not indicated in pregnant women due to the high risk of vena cava syndrome and subsequent decrease of placental flow. These risks can be reduced if the restraint is done with preference for patient in prone to the left side [50]. It is important to change the position of the pregnant woman frequently to reduce the possible obstruction of the inferior vena cava. In addition, for all restrained pregnant women, continuous monitoring by a health care professional in proximity is required. Careful attention should be taken while using mechanical restraints in pregnant women, mainly during the second and third semesters, to avoid undue pressure on the uterus. Monitoring of fetal heart rate and movement should be done frequently [50, 51].

Suicidal behavior

The prevalence of pregnancy and postpartum suicidal ideation varied extensively across the studies ranging from 3–33% [52]. Suicidal ideation is a complex and multicausal phenomenon, since it is usually the result of a mental disorder that can be treated.

The suicidal attempt is the final event of a network of factors that have interacted during the individual's life, in varied particular and sometimes unpredictable ways. Completed suicide is one of the leading causes of maternal death during pregnancy and peripartum in developed countries [21, 53].

This complexity includes genetic, biological, psychological, social, historical, and cultural factors [43, 54]. Understanding these factors the network of events is essential for the healthcare provider to be able to provide adequate care to patients who have attempted suicide or who are at higher risk [55]. Contrary to the idea that pregnancy and childbirth might have a protective effect against suicide [56], recent studies have indicated that pregnancy and the postpartum are vulnerable times for women, especially those with previous history of mental health conditions [49].

Although the prevalence of suicidal attempts and the rates of death by suicide are relatively low during pregnancy (in mothers with depression), the consequences of a suicidal attempt are medically and psychologically devastating for the mother [57]. Notably, postpartum suicidal behaviors (including suicidal ideation, attempts, and completed suicide) are often preceded by antepartum suicidal behavior [58].

This pattern of prepartum conditions that predict postpartum risks and that persist well beyond the prenatal period is also seen in maternal mood, anxiety and stress disorders [52, 59]. Hence, the antepartum period represents a critical period and important opportunity for suicide risk reduction and prevention [52].

Management:

1. **Rule out other emergencies** as trauma, acute intoxication, obstetric emergencies.
2. **Assessment of risk and protective factors.** One of the main challenges in approaching suicidal behavior is to predict which patients will attempt again. To date, there are no precise tools to predict suicide. Therefore, in the clinical evaluation, it is important to estimate the severity of the patient according to the presence of risk factors [54, 60]. Notable risk factors include, but are not limited to: suicidal ideation, suicidal attempt, and a plan for suicide [54, 60]. It has been shown that the frequency of suicidal ideation may be up to 33% of the pregnant population [57], which demonstrates that suicidality is common in this period [21, 53, 61]. In addition, among pregnant women and puerperal women, a previous history of suicide attempt, previous history of severe psychiatric illness and hospitalization are important risk indicators for suicidal behavior. During hospitalization, women with a psychiatric disorder were at a 27.4-fold increased risk, and those with a substance use disorder were at a 6.2-fold

increased risk, and those with a dual diagnosis were at an 11.1-fold increased risk of postpartum suicide attempt compared with controls [62].

3. **Patient safety.** In the perinatal period, most women who complete suicide do so in the third trimester of pregnancy or in the last three months of the baby's first year of life [21]. Women in the perinatal period tend to use more violent methods to commit suicide, such as hanging, jumping from a great height, or being run over [21, 49]. Thus, attention should be paid to the possibility of access to tools that increase the risk of lethality from a suicide attempt, such as having access to weapons or potentially lethal medications [63]. Socioeconomic factors may contribute to the manifestation of suicidal behavior, such as lack of family support, absence of a partner, financial difficulties, unplanned pregnancy, teenage pregnancy, history of domestic violence and alcohol/illicit drug use [49, 64]. Protective factors for suicidal outcomes have also been previously identified: planned cesarean delivery, marital satisfaction, being a first-time mother, and harmony with mother-in-law [54, 60].

4. **Safety plan.** More frequent follow-up consultations should be carried out, and the involvement of family members and other health professionals is encouraged (and in some cases, essential) to ensure the safety of the mother-infant pair [65]. Psychotherapeutic strategies are also indicated, especially Cognitive Behavioral Therapy and Interpersonal Psychotherapy [65]. The goal of the safety plan is to ensure that the patient and her support network are aware of the patient's risk factors, impending warning signs and ways to access support, all the while providing closer support and monitoring. If the patient does not show up, the care team should try to actively contact the patient. At each visit, the safety plan is reassessed. The use of medications in severe cases, involving the presence of suicidal behavior, is recommended [55]. During pregnancy, evidence-based treatment of maternal psychopathologies is a protective factor for outcomes related to suicide [35]. Risk-benefit models for decision-making on the use of psychiatric drugs in pregnancy should be used, with the patient encouraged to discuss with family or, if appropriate other supports in her life [35]. Child protection services should be notified in cases of risk for the baby or other children in the home.

We should discuss the possibility of psychiatric hospitalization if the patient has imminent risk of suicide. Admission to a unit specialized in the care of women during pregnancy and peripartum exist, although these are not common [66]. Pregnant and postpartum women should be monitored closely, not only for the high risk of suicide when depressed or with psychotic symptoms, but also due to the risk of infanticide or filicide [21,

35]. In some cases, hospitalization for the mother-infant pair should be prioritized if at all possible, so that bonding issues can be addressed [35].

In severe cases of peripartum psychosis or episodes of depressed or manic mood, electroconvulsive therapy (ECT) is a well-established treatment option, [60, 67] especially when traditional treatments could delay recovery, interrupting the proper establishment of the mother-infant bond [67].

Despite the rapid effect and efficacy of electroconvulsive therapy, a systematic review reported adverse events such as reduced fetal heart rate, uterine contractions and premature birth (born between 29 and 37 weeks of gestation) in almost one third of cases (29%) [68].

Psychosis and mania

The incidence of peripartum psychosis is 1–2 per 1,000 births [2]. A psychotic episode in the peripartum period may be new or recurrence of pre-existing mental illness. This category includes known bipolar illness relapse, first episode affective psychosis during pregnancy/peripartum, isolated peripartum psychosis, and schizophrenia spectrum disorders.

For this reason, hospitalization is indicated in these cases [38]. In an study, women who have bipolar disorder are seventy times more at risk of worsening symptoms in the postpartum [69]. On the other hand, Wessseloo et al. observed that one-third of women at high risk experience a postpartum relapse. The overall postpartum relapse risk was 35%.

Patients with bipolar disorder were significantly less likely to experience severe episodes postpartum than patients with a history of postpartum psychosis. In women with bipolar disorder, postpartum relapse rates were significantly higher among those who were medication free during pregnancy than those who used prophylactic medication [70].

Untreated bipolar spectrum illness is associated with unwanted or unplanned pregnancies, risk for poorer physical status of mother and fetus/baby, increased distress for mother and family, disruption of the maternal-infant bond, maternal suicide and filicide, and negative child outcomes. The overall relapse risk for women with only peripartum onset psychoses is 31% [71]. Peripartum psychotic disorder, whether new or pre-existing, may also be associated with the use of high-risk substances

and behaviors that increase exposure to sexually transmitted diseases, abandonment of treatment, and self-neglect [38].

Management

When counseling pregnant women on management options, mental healthcare professionals must explain the risks of different treatment options accurately, balanced against the risk of not treating the mental disorder, while acknowledging the limits of the knowledge available. This includes the risk of not treating the mental disorder (risks to the woman, to the fetus and to the infant from untreated disorders as well as risks to other children, partners, and family members), the risk of treating the disorder and the underlying risk of congenital malformations.

Main risk factors for peripartum psychosis include a history of bipolar disorder, history of schizophrenia and other psychotic disorders, prior episode of peripartum psychosis, non-adherence, medication changes, depression with psychotic features in the peripartum, primiparity, and increased psychological stress [2].

Regarding clinical presentation, although the psychotic symptoms are often the most dramatic manifestation, women also present with mood symptoms (mania, depression, or mixed mood). Others possible symptoms include disorganized behavior, obsessive thoughts, delusions, hallucinations, and notable perplexity: Delusions may be mood incongruent and are often related to the infant. Marked fluctuations in the intensity of symptoms, suicidality, thoughts of harm to self and/or infant/other children are also not rare [72].

During the assessment and the first attendance in emergencies, situations of greater risk, such as psychomotor agitation, suicidal behavior, and physical complications must first be addressed. The patient is highly likely to need to remain under observation (at minimum) or require hospitalization. Ideally, this should occur in a setting that includes access to a psychiatrist and obstetrician. Other specialties may be consulted if necessary. In the case of pregnant women or women who have recently given birth, even if there are no apparent symptoms or physical signs of disease or partum complications, the assessment of the obstetrician is necessary.

In the treatment of psychoses during pregnancy it is recommended to use antipsychotics in the lowest possible dosages and pharmacokinetic changes

that occur in pregnant women should be considered when prescribing the medication. In general, it appears that antipsychotics are, for the most part, relatively safe for use in pregnancy and their non-use, when indicated for serious mental problems represents a much greater risk, including suicide and infanticide. Maternal weight gain, greater fetal birth weight and hyperglycemia may occur, which must be continuously monitored.

Regarding the treatment of peripartum psychosis, the largest evidence base points to the use of lithium, antipsychotics, and ECT [71]. Lithium or

antipsychotics in monotherapy can be used for treatment, however, the use of lithium in monotherapy was associated with significantly lower relapse numbers when compared to antipsychotic monotherapy. As with non-peripartum women, serum lithium should be targeted to between 0.8 to 1.2 mmol/L and its use is recommended for 9 months [72].

For women with a history of peripartum psychosis, prophylactic treatment with lithium, right after delivery, is considered the first-line treatment [2]. For bipolar depression lamotrigine can be a safer option for pregnancy and breastfeeding [15].

A study observed from 185 cases in the postpartum compared 185 cases without postpartum (46% with psychosis in both groups), that more cases (87.0%) than comparison group subjects (73.5%) responded to ECT [73]. Adjusted binary regression analysis revealed that more severe symptoms prior to treatment were the only statistically significant predictor of response [73].

Regarding breastfeeding, despite its indisputable benefits, its continuity must be evaluated, weighing the risks and benefits in relation to the treatment of psychoses [74]. Antipsychotic levels in breast milk are generally low, but there is a significant lack of data on long-term outcomes and possible side effects, including developmental effects and extrapyramidal side effects. Women should be counseled about this lack of data, and exposed babies should be monitored carefully by a pediatrician [74].

The use of benzodiazepines may be done for a limited period, giving preference to those with a short half-life and watching for signs of sedation in the baby [8]. In cases of women recovering from postpartum psychosis,

breastfeeding at night is not advised, as interruption of sleep can increase the risk of not improving or exacerbating the disorder [8].

All women with depressive symptoms should be screened for bipolar disorder during pregnancy and the peripartum period [15]. Standardized screening tools such as the Mood Disorder Questionnaire alone or in conjunction with the Edinburgh Postnatal Depression Scale are useful [75].

A longitudinal study conducted in a tertiary care center found a high risk of recurrence during pregnancy: 85% of pregnant women with bipolar disorder who discontinued a mood stabilizer and 37% of those who were maintained on one or more mood stabilizers experienced a mood episode—predominately depressive or mixed—during pregnancy [15]. The risk of relapse is highest in women who also experienced a mood episode during pregnancy and those who are not on prophylactic treatment [15].

Decisions about breastfeeding may be discussed with a pediatrician or psychiatrist with expertise in perinatal mental health. The medication choice must consider the most updated information about medication risks, including relative infant dose (RID) in the breastmilk if breastfeeding is being considered. Education about early recognition of drug toxicity and a requirement for ongoing monitoring of infants is also critical [15, 76]. A recent systematic review suggested quetiapine and olanzapine as preferred choices for breastfeeding, considering their relatively lower infant dosages [14, 15].

Replacing or supplementing breast milk with formula can also be considered. Although there are many benefits to breastfeeding, associated sleep disruption may increase the risk of mood episodes in women with bipolar disorder. If possible, bottle-feeding at night by the woman's partner or a support person can be beneficial to allow the woman to maintain a better sleeping schedule. In women with peripartum psychosis or mania, breastfeeding may be a risk, and therefore may not be indicated, as the mother may be too disorganized to safely breastfeed [15]. Nevertheless, it can proceed in most cases with close monitoring by a qualified healthcare provider.

Severe depression

Depression is the mental health condition that most affects perinatal women and mothers worldwide. In general, about 10% of pregnant women and 13% of women who have given birth experience a mental disorder,

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primarily depression. In developing countries like India, this is even higher, i.e., 15.6% during pregnancy and 19.8% after childbirth [77]. Pregnancy and postpartum depression is considered a major health public issue [77-82].

There are several consequences of this pathology. These negligence in feeding the baby; "accidental" injuries to the baby; depression in the partner; divorce; lower cognitive development of the child; and behavioral disorders with manifestations in childhood and possibly beyond. One of the most feared consequences of peripartum depression is suicide. Untreated

antepartum depression is one of the strongest risk factors for peripartum depression (PPD), and PPD has potentially devastating consequences, including suicide and infanticide.8 Suicides account for up to 20% of all peripartum deaths and represent one of the leading causes of peripartum mortality [8].

Management:
An efficient way to identify symptoms of depression in peripartum is the application of self-report scales, such as the Edinburgh Perinatal Depression Scale (EPDS). Once perinatal depression is diagnosed, treatment should involve three types of care: gynecological, psychiatric, and psychosocial.

Regarding psychiatric care, treatment with antidepressants is indicated for cases in which depression is compromising the mother's function and well-being. The decision to prescribe a pharmacological agent must be made based on the history of the disease and the following risk factors: risk of the fetus resulting from exposure to the drug; risk of untreated illness for the mother and fetus.

Selective serotonin reuptake inhibitors (SSRIs) are the most prescribed antidepressants for the treatment of depression throughout pregnancy, as they are not significantly associated with an increased risk for fetal malformations [8, 23]. In severe cases (presence of suicidal ideation or psychotic symptoms) the use of Electroconvulsive Therapy (ECT) may be indicated.

In cases of psychotic manifestations associated with unipolar depression, quetiapine has some favorable characteristics: antidepressant properties;

adjunct drug of choice in refractory depression; and lower levels of placental passage than haloperidol, olanzapine and risperidone [11].

Psychological treatments, including CBT and IPT, may be an alternative for mild and moderate depression, and association between SSRIs with psychological treatment in moderate and severe depression [35, 83].

Substance use disorders

There is widespread agreement that the first 1,000 days following conception are critical for laying the foundations of optimum health, growth, and neurodevelopment. This period covers pregnancy, delivery, and breast-feeding, ending roughly on the infant's 2nd birthday [84].

According to National Survey on Drug Use and Health, in the United States 19.5 million females (15.4%) aged 18 or older have used illegal drugs in the past year [85]. Drug use during pregnancy, including alcohol, can cause numerous long and short-term health problems for both mother and child.

Substance use among pregnant women has increased steadily in the past decade [51]. It is estimated that, in the United States, more than 4.4% of women misuse one or more substances during pregnancy [86]. Risk factors for drug use during pregnancy include prior drug use, unwanted pregnancy, younger age, unemployment, lower level of education, violence, childhood trauma, easy accesses and lack of information of the consequences [86].

Furthermore, the stigma of alcohol and drug use during pregnancy is so widespread that it is often assumed that a pregnant woman is not using. This is often the case even among healthcare professionals. A recent study showed that a pregnant woman presenting to an Emergency Department is 75% less likely to be tested for drug use than a non-pregnant woman of similar age [87].

In 2015, 3.4% of pregnant women in the US reported using cocaine in the past 30 days; cocaine is the second most commonly used drug among

pregnant women [85]. Maternal complications of cocaine use in pregnancy include cardiovascular disorders such as hypertension, myocardial infarction and ischemia, renal failure, hepatic rupture, cerebral ischemia/infarction, and maternal death [88, 89].

Rates of cannabis use are increasing among pregnant and non-pregnant women in the United States. In 2014, 3.85% of pregnant women mentioned using cannabis in the previous month [90, 91]. THC and other substances are known to cross the placental wall and are excreted in breastmilk [92]. Cannabis use may be associated with slow growth, spontaneous preterm birth, stillbirth, and admission to the neonatal intensive care unit on birth [93, 94].

Pregnancy might be a window of opportunity for behavioral changes, and it is important to screen pregnant women for alcohol and substance abuse. Behavioral measures must be the focus of treatment as there is limited data on the use of drugs to treat alcohol dependence (e.g., disulfiram, naltrexone, acamprosate) during pregnancy. Physicians must carefully weigh the risks of using such drugs versus alcohol use [84, 87, 94-96].

Management

For women in acute intoxication support, avoid benzodiazepines and use if agitation. It must exclude association with trauma and clinical complications.

For women with alcohol withdrawal or cocaine or stimulant intoxication, benzodiazepines are the medications of choice in the treatment of alcohol withdrawal in the general population and by extrapolation, in pregnant patients. The risks with short-term administration of benzodiazepines, as is typical for alcohol detoxification, are likely to be even lower (if its use is restricted to the rapid improvement of the signs and symptoms of withdrawal). The use of benzodiazepines close to delivery can cause floppy infant syndrome in the baby or even withdrawal symptoms.

However, the potential harms of untreated withdrawal to mother and infant must, therefore, be balanced against the potential risks of benzodiazepine use during pregnancy and breastfeeding. In the case of severe agitation and psychotic symptoms, the use of antipsychotics is also justified.

Dependence

The approach to addiction during the last trimester and during breastfeeding, as well as alcohol, should be focused on the multidisciplinary non-drug approach.

Women (who are regular substance users) should be provided with concurrent addiction counseling and encourage to remain abstinent while nursing and be provided with sufficient information about the increased risks of adverse neonatal effects (e.g., seizures, tachycardia, and irritability). In selected cases cocaine can be measured in milk and, when clinically indicated (e.g., suspected adverse effect), also in neonatal blood.

Patient and Child Safety

Perhaps one of the most difficult challenges for psychiatrists and obstetricians is to determine whether perinatal patients pose a danger to themselves or their children. As the rates of suicide and infanticide are high in cases of severe cases, it is important to assess such risk and remember that it is always better to err on the side of caution.

Women with mental illnesses can be and usually are excellent mothers, but those with acute episodes, with impaired insight and volition may be in danger of harming their children deliberately or through negligence caused by the mental illness [64, 65].

In the face of a female patient of reproductive age, the clinician must always be aware of the possibilities of pregnancy and breastfeeding. Specifically, the psychiatric manifestations that pose the greatest risk to women in the perinatal period and, therefore, can be actively questioned: [97, 98]

• abortive ideation
• risk of infanticide
• psychiatric symptoms and signs related to the pregnancy itself (e.g., intense fear of childbirth; tokophobia) and puerperium (e.g., intense fear of unfitness for the mother's routine)
• hostile thoughts or attitudes towards the fetus and baby (e.g., aggression of the pregnant woman to her abdominal region)
• delusional ideas about pregnancy and postpartum

Conclusion

Psychiatric emergencies in the pregnancy and peripartum period are a challenge not only for the psychiatrist, but for other disciplines such as obstetrics. Literature remains scarce on the subject and most decisions are based on the empirical experience of the professional or based on literature from other groups.

When in doubt, the psychiatrist, in the face of an emergency, should consider the best conduct that provides (as far as possible) protection to the patient and her baby. We present in Figure 1 and 2 two flowcharts to help in the decision making for psychiatric emergencies in pregnant and postpartum. The summary information of this consensus is in Tables 1, 2, and 3 and in Figures 1 and 2.

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Table 1. Main cautions in pregnancy and postpartum psychiatric emergencies

01. The best place for emergency care for pregnant women is an emergency room or hospital that provides 24-hour obstetrics and psychiatry.
02. The assessment of psychiatric emergencies requires general physical, gynecological-obstetric, and psychiatric evaluation in all cases.
03. Exclude medical causes /substance intoxication or withdrawal [15, 19, 28, 34]
04. Rapid tranquilization if indicated [13-15, 66]
05. Assess suicidal risk, [28, 34], agitation, aggression to others, [15, 19] delusions involving infant, risk of harm to baby/others.
06. Apply scales to assess the severity of symptoms.
07. Children: determine if it is or not possible to admit patient with baby
08. When choosing medication, consider expected time of use, risk versus benefit and pharmacokinetic and pharmacodynamic issues.
09. Mobilize social support.
10. Inform the patient and family about the therapeutic proposal and follow-up.
11. Determine if continuous/ongoing monitoring or hospitalization is necessary [15, 19, 28, 34]
12. Record the information obtained in the medical record.

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Table 2. Suggested medications for rapid tranquilization in pregnancy and lactation

Medication	Dosage	Can repeat	Maximum dosage	Observation
Antipsychotics				
PO/OS/ODT risperidone	2-4mg	1h	8mg	3rd trimester: risk floppy baby and extrapyramidal syndrome
IM Haloperidol	2,5-7,5mg	30min	10mg	3rd trimester: risk floppy baby and extrapyramidal syndrome
Benzodiazepines				
PO, OS clonazepam	2mg	1h	6mg	3rd trimester: risk floppy baby and withdrawal syndrome
PO, IV diazepam*	10mg	1h	40mg	3rd trimester: risk floppy baby and withdrawal syndrome
PO, IM lorazepam	2-4	1h	4mg	3rd trimester: risk floppy baby and withdrawal syndrome

* Exclusively for alcohol withdrawal, cocaine intoxication, or seizures

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Table 3. Recommendations for management of psychiatric emergencies in pregnancy and postpartum

1. The best place for emergency care for pregnant women is an emergency room or hospital that provides 24-hour obstetrics and psychiatry.
2. The evaluation of psychiatric emergencies requires general physical, gynecological-obstetric and psychiatric evaluation in all cases.
3. Pharmacotherapy should consider the benefits of improving the behavior of the pregnant woman and the harm to the mother and baby according to the stage of pregnancy or postpartum.
4. Medications used in a short period of time in an emergency do not require as much concern as harm, since the behavior that requires care is at greater risk than treatment.
5. However, medications for long-term use require careful planning.
6. The most suitable approaches in emergencies during pregnancy and postpartum are listed in figure 2.

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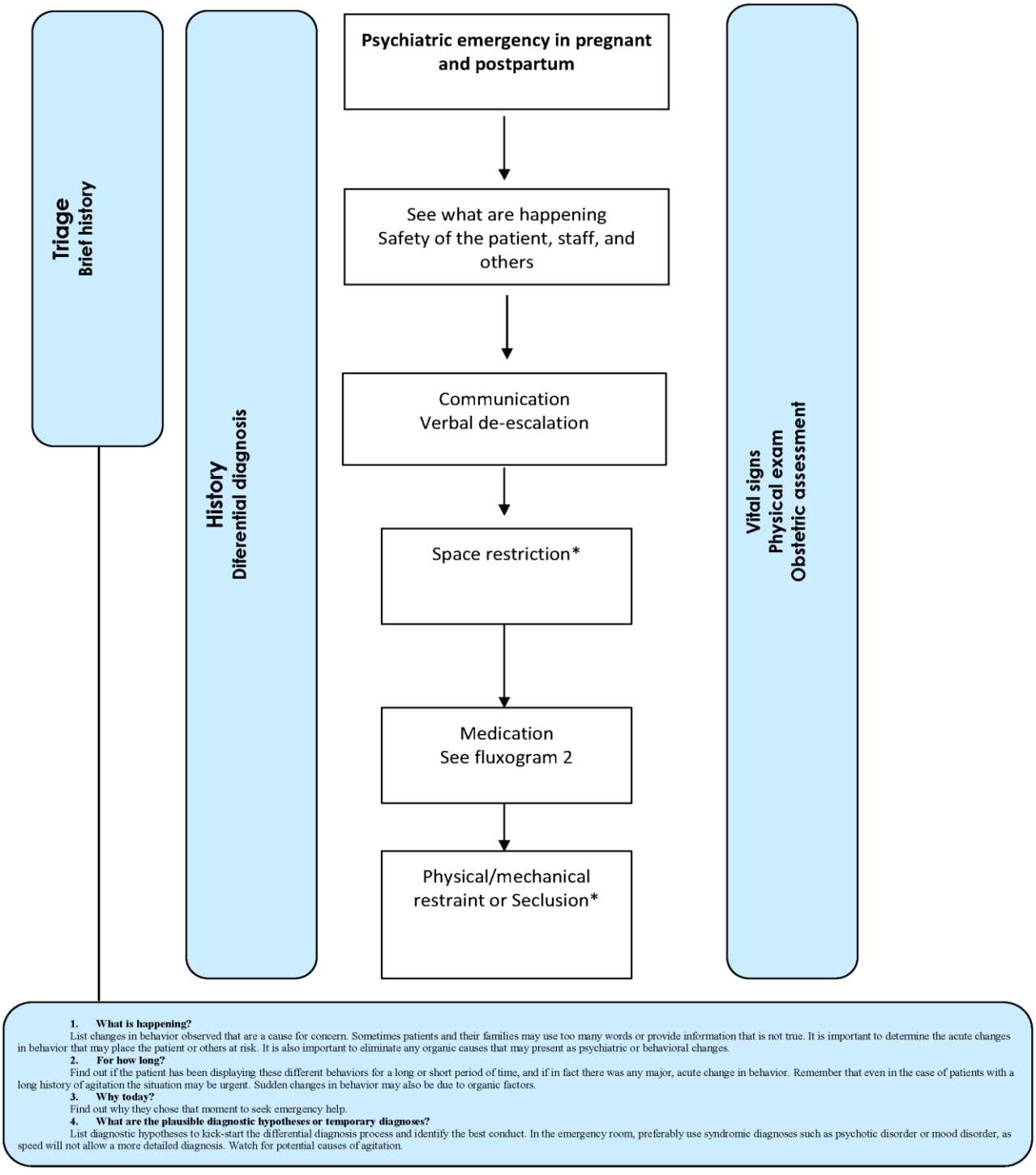

* Few data to support. Use only if there is no another way.

Figure 1. General management of psychiatric emergency in pregnancy and postpartum

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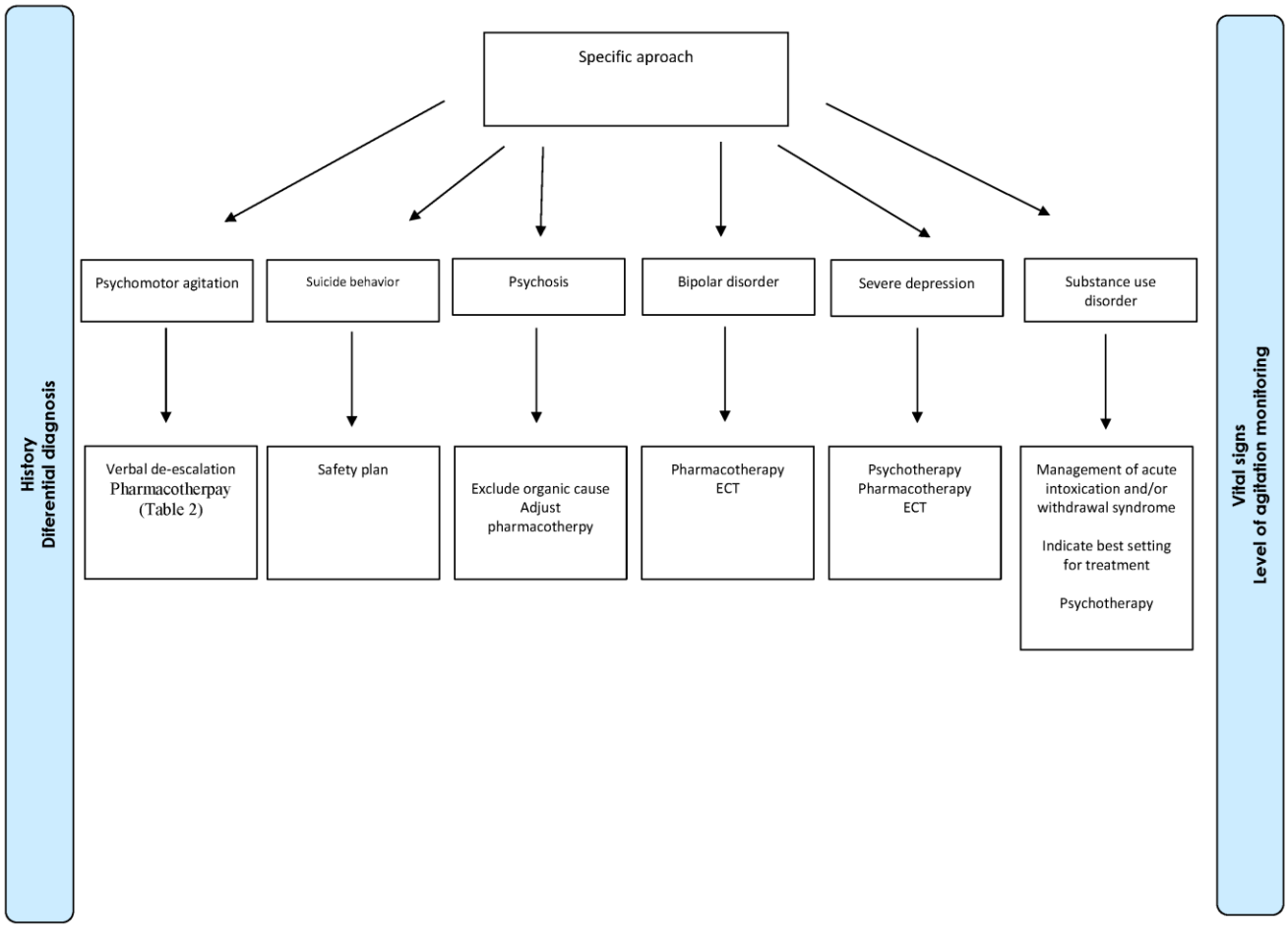

Figure 2. Specific aproach for psychiatric emergencies in pregnancy and postpartum

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