Perinatal Bipolar Disorder

Amritha Bhat MD, MPH
Psychiatry and Behavioral Sciences
University of Washington

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General Disclosures

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Speaker Disclosures

- PAL for Moms phone consultation line for providers

  State of Washington Health Care Authority

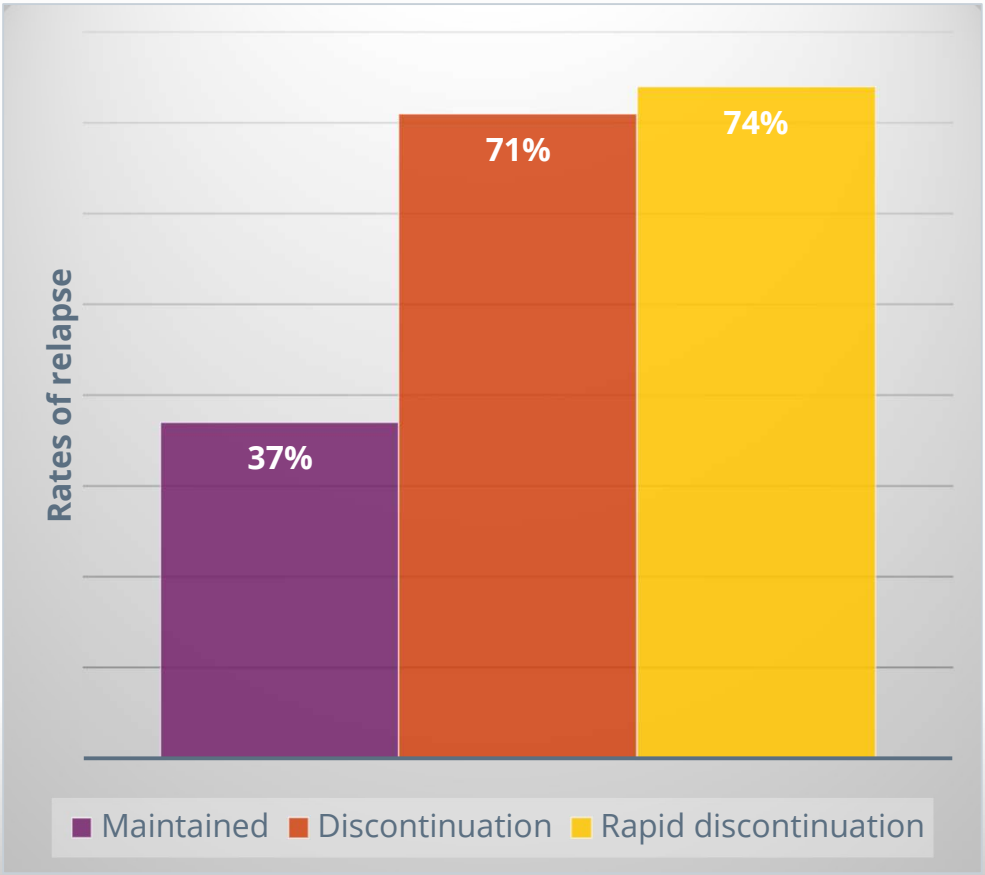
  206-685-2924 or 1-877-PAL4MOM, M-F 9-5

- Perinatal Psychiatry Clinic

Learning Objectives

- Describe the assessment and diagnosis of bipolar disorder in the perinatal period
- Compare the risks of untreated bipolar disorder with the risks of psychotropic medication use during pregnancy and lactation
- Describe measurement-based care for perinatal bipolar disorder
- Consider non-medication interventions in treatment plans for bipolar disorder during pregnancy and postpartum
- Conduct detailed informed consent discussions with pregnant and breastfeeding women regarding psychotropic medications commonly used for bipolar disorder

Risk of Relapse in Pregnancy



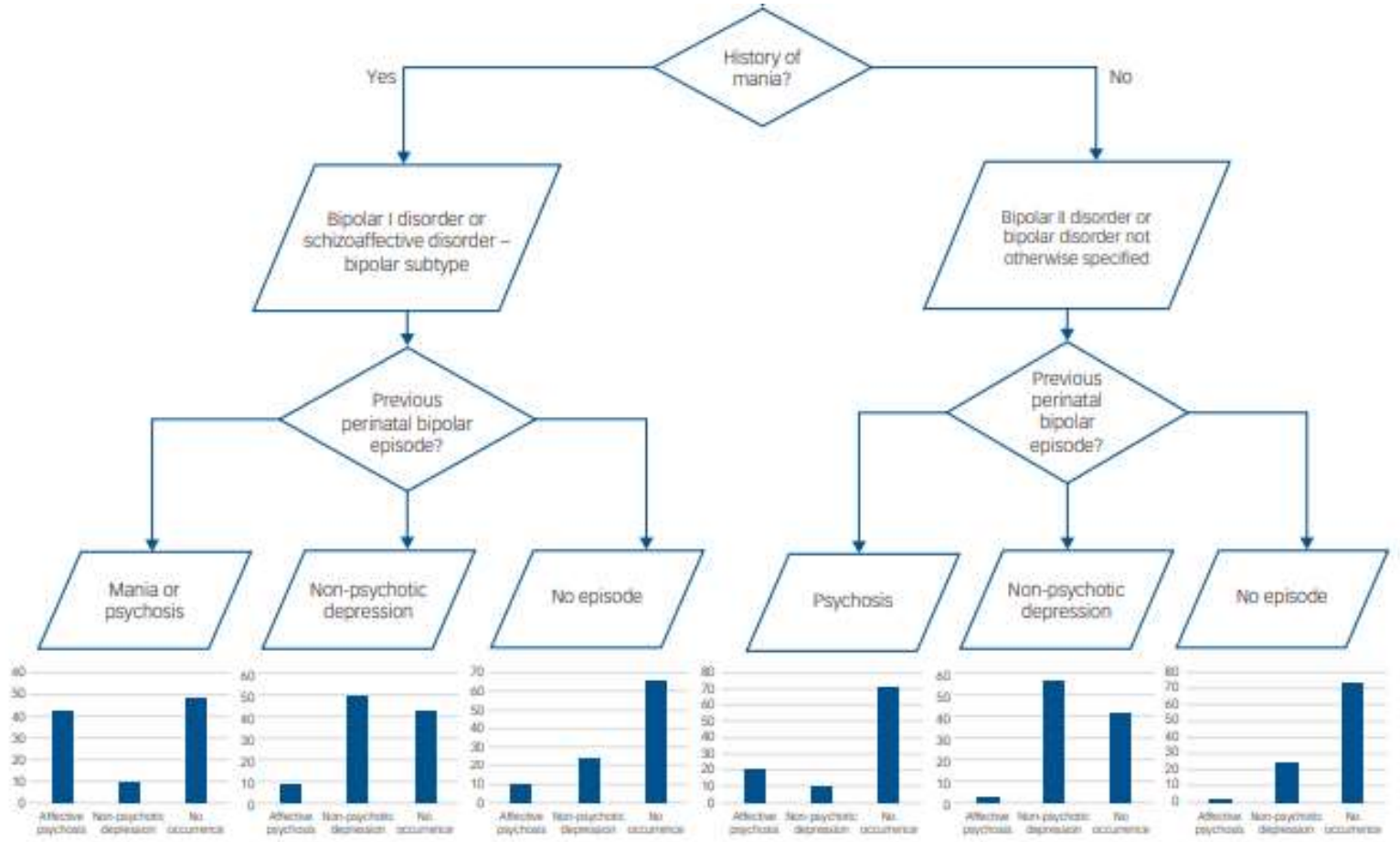
74% episodes depressive or mixed

47% in first trimester

Risk Factors for relapse
Unplanned pregnancy
Younger age of onset
Rapid cycling
Mixed episodes
Shorter stability
Polytherapy
Antidepressants

Viguera et al, 2000

Risk Assessment of Perinatal Episodes



diFlorio et al, 2018

Screening and diagnosis

- MDQ (Mood Disorder Questionnaire) Sensitivity 87% Specificity 85%
- Other measures:
  - **CIDI**
  - **Altman Self-Rating Mania Scale (patient rated)**
  - **Bech-Rafaelsen Mania Rating Scale (clinician rated)**
  - **Bipolar Inventory of Symptoms Scale (patient rated).**
  - **PHQ-9, EPDS, QIDS-SR**
- Be aware of racial disparities in diagnosis and treatment

Cerimele et al, 2019

MDQ

Instructions: Check (✓) the answer that best applies to you.
Please answer each question as best you can.

	Yes	No
1. Has there ever been a period of time when you were not your usual self and...		
...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?	◯	◯
...you were so irritable that you shouted at people or started fights or arguments?	◯	◯
...you felt much more self-confident than usual?	◯	◯
...you got much less sleep than usual and found you didn't really miss it?	◯	◯
...you were much more talkative or spoke faster than usual?	◯	◯
...thoughts raced through your head or you couldn't slow your mind down?	◯	◯
...you were so easily distracted by things around you that you had trouble concentrating or staying on track?	◯	◯
...you had much more energy than usual?	◯	◯
...you were much more active or did many more things than usual?	◯	◯
...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?	◯	◯
...you were much more interested in sex than usual?	◯	◯
...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?	◯	◯
...spending money got you or your family in trouble?	◯	◯
2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time? *Please check 1 response only.*	◯	◯
3. How much of a problem did any of these cause you — like being able to work; having family, money, or legal troubles; getting into arguments or fights? *Please check 1 response only.* ◯ No problem ◯ Minor problem ◯ Moderate problem ◯ Serious problem		
4. Have any of your blood relatives (ie, children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?	◯	◯
5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?	◯	◯

This questionnaire should be used as a starting point. It is not a substitute for a full medical evaluation. Bipolar disorder is a complex illness, and **an accurate, thorough diagnosis can only be made through a personal evaluation by your doctor.**

CASE

35 yo married female G1 at 16 weeks gestation presents with depression, PHQ-9 of 12, no suicidal ideation. She has had 1 depressive episode in the past. She tells you she did not tolerate sertraline or citalopram. When asking for more details on her response to sertraline and citalopram she tells you she became very agitated, felt like she was on speed, and stayed up all night for 4 nights, cleaning the house. What would you recommend?

A. Lamotrigine

B. Lithium

C. Venlafaxine

D. Watchful waiting

Lamotrigine

- Not inferior to lithium in the prevention of severe PP episodes
- Prospective study from teratology service (median dose 200 mg/d): No increase in MCM.
- 29% needed dose increase during pregnancy (monthly monitoring)
  - **If dose was increased during pregnancy, taper to pre pregnancy dose within 2 weeks:**
    - decrease by 25% immediately PP
    - decrease every 3 -4 days until prepregnancy dose is reached (check pre pregnancy euthymic level)
- No neurodevelopmental disorders in children exposed to in utero lamotrigine (up to 6 years)

Clark et al, 2018

CASE

25 yo female with diagnosis of bipolar disorder type 1 , onset at age 14, 5 hospitalizations for mania or severe depression with suicidal ideation, stable on 1200 mg lithium for the past year. She wants to get pregnant in the next 6 months. What would you recommend?

A. Cross taper to lamotrigine

B. Continue lithium

C. Stay off lithium for the first trimester

D. Postpone thinking about pregnancy

Lithium: Congenital Malformations

- ? Ebstein's anomaly
  - **Baseline 1 in 20,000; Lithium 1 in 1000**
- Risk for cardiac malformations: adj RR of 1.65 (95% CI, 1.02-2.68)
- No significant difference in major cardiac malformations (2.1% (0.5%-3.7%) vs 1.6% (1.0%-2.1%).
- Higher odds of
  - Any cong anomaly (4.1%, OR 1.8, NNH 33)
  - Cardiac anomaly (1.2%, OR 1.86, NNH 71)

Munk Olson et al, 2018; Fornaro et al 2020

Lithium: Efficacy

- More effective than no lithium in preventing postpartum relapse (OR 16, 95% CI=0.03-0.89; NNT=3)

Fornaro et al 2020

Lithium and pregnancy outcomes

- No increased risk of miscarriage?
- Not associated with preeclampsia, GDM, PPH, CS.
- Increased risk for neonatal readmission within 28 days of birth for lithium (pooled prevalence 27·5% [95% CI 15·8-39·1] vs 14·3% [10·4-18·2])

Poehls et al, 2020

Prescribing lithium

- Pregnancy:
  - **If possible, reduce dose in first trimester**
  - **Twice daily dosing to minimize peak levels/ side effects**
  - **Blood level monitoring – monthly up to 34 weeks; weekly thereafter; Increase dose as required.**
  - **Fetal anomaly US (fetal cardiac scanning) at 16 – 20 weeks GA**
- Labor and Delivery:
  - **Lithium level when patient presents for delivery and 24 hours after delivery**
  - **Adequate hydration; Considerations for pain relief**
  - **Cord blood Li, TSH, Free T4**
  - **Pre-conception dose once medically stabilized**
- Postpartum
  - **Consider a higher target therapeutic lithium level for the 1st PP month (0.8-1mmol/L)**
  - **Twice weekly lithium blood levels in 1st 2 PP weeks**
  - **Breastfeeding generally not recommended**

Clark et al, 2018

CASE

35 yo married female G1 at 6 weeks gestation presents with severe depression, PHQ-9 of 21, no suicidal ideation. She has had 5 depressive episodes in the past, one leading to psychiatric hospitalization for suicidal ideation, and 2 episodes of hypomania. What would you recommend?

A. Lamotrigine

B. Lithium

C. Venlafaxine

D. Quetiapine

Second generation antipsychotics and malformations

- No increased risk:

  Aripiprazole, Olanzapine, Quetiapine
- Minor increased risk:

  Risperidone, Paliperidone (RR 1.26)
- Insufficient data:

  Amisulpiride, Asenapine, Lurasidone,

  Sertindole

Mood stabilizers and lactation

Medication	Relative infant dose	Adverse effects	Compatibility
Lithium	3.1- 69	Hypotonia, lethargy, hypothermia, inversion of ECG wave	-
Valproate	0.1 – 3.9	Thrombocytopenic purpura, anemia, and reticulocytosis	+
CBZ	1.1-7.3	Poor suckle, poor weight gain, sedation, transient hepatic dysfunction	+
Lamotrigine	1.8-21.1	Sedation, respiratory suppression	+

Hypnotic Medications

Medication	Pregnancy	Lactation/development
Lorazepam	No inc risk of cong malformations; (poss incr when used with SSRIs). Use near term – floppy baby. Unclear data on long term neurodevelopment	Low levels in breastmilk, no adverse effects in breastfed infants with usual dosages
Clonazepam	No inc risk of cong malformations; (poss incr when used with SSRIs). Use near term – floppy baby. Unclear data on long term neurodevelopment	Can cause sedation, esp in younger, excl breastfed infants. Monitor for drowsiness, wt gain, milestones
Diphenhydramine / hydroxyzine	Inconsistent reports of malformations	Drowsiness, irritability in breastfed babies. May interfere with lactation
Doxylamine	No increase in malformations	Sedation, irritability; no effects on development at 3-7 yo
Mirtazapine	Not expected to inc rate of malformations	Limited information; small amounts in breast milk
Trazodone	Not expected to inc rate of malformations	Limited information; small amounts in breast milk
Zaleplon	Limited information; no reports of malformations	Limited information; small amounts in breast milk
Zolpidem	Not expected to inc rate of malformations. ? Inc rate of PTB and LBW	Limited information; ; small amounts in breast milk

Always ask about co sleeping when prescribing sedating medications!

Non medication interventions

- Sleep!
- CBT-I
- CBT
- IPSRT
- Light therapy
- ECT

Risk- Risk Assessment

Bipolar Disorder

Anti-psychotics; Mood Stabilizers

- Poor prenatal and self care, subs abuse, fetal abuse or neonaticide (PPP)
- Prematurity, microcephaly, neonatal hypoglycemia
- Longer term effects due to poor bonding

- GDM, higher rates of CS
- LBW, preterm
- Teratogenicity
- Neonatal syndromes
- Long term neurocognitive outcomes

Factors to Consider in the Treatment of Perinatal Bipolar Disorder

- Patient's treatment preferences
- Current time of gestation; Fetal safety of medication
- Past illness course, rapid cycling, peripartum episodes, response to medication
- Comorbid psychiatric disorders
- Preconceptional duration of stability
- Access to psychotherapy
- Strength of social network

Thomson et al, 2018; Yatham et al, 2018

Take home points

- Untreated Bipolar Disorder is associated with risks for the mother and baby
- Counsel re smoking, nutritional intake and prenatal care
- Evaluated for anxiety disorders, OCD, and substance use disorder; assess for thoughts of harm to self and the newborn
- Use monotherapy where possible
- Acute treatment of perinatal bipolar depression: lamotrigine or quetiapine
- Acute treatment of mania or mixed: quetiapine, benzo, lithium
- Maintenance: Lamotrigine, lithium, SGA
- Individual risk benefit analysis is important

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Questions/Contact Information

Feel free to contact me at:
amritha@uw.edu