Perinatal Bipolar Disorder

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

November 6, 2019

General Disclosures

The UW Department of Psychiatry and Behavioral Sciences gratefully acknowledges receipt of anonymous philanthropic support for this activity – working to expand access to perinatal behavioral health services throughout Washington State.

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

- UWMC Perinatal Psychiatry Clinic

Learning Objectives

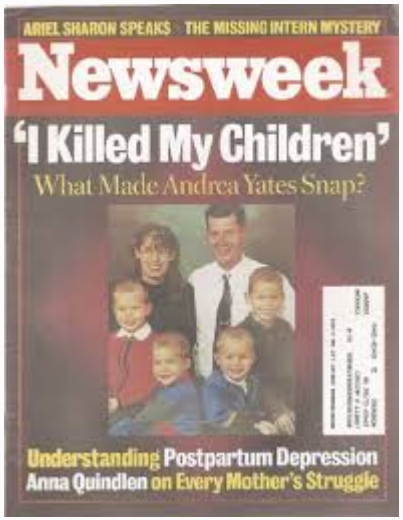
- Describe the differential diagnosis of bipolar disorder in the perinatal period
- Compare the risks of untreated bipolar disorder with the risks of psychotropic medication use during pregnancy and lactation
- Describe measurement-based care for perinatal bipolar disorder
- Consider non-medication interventions 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

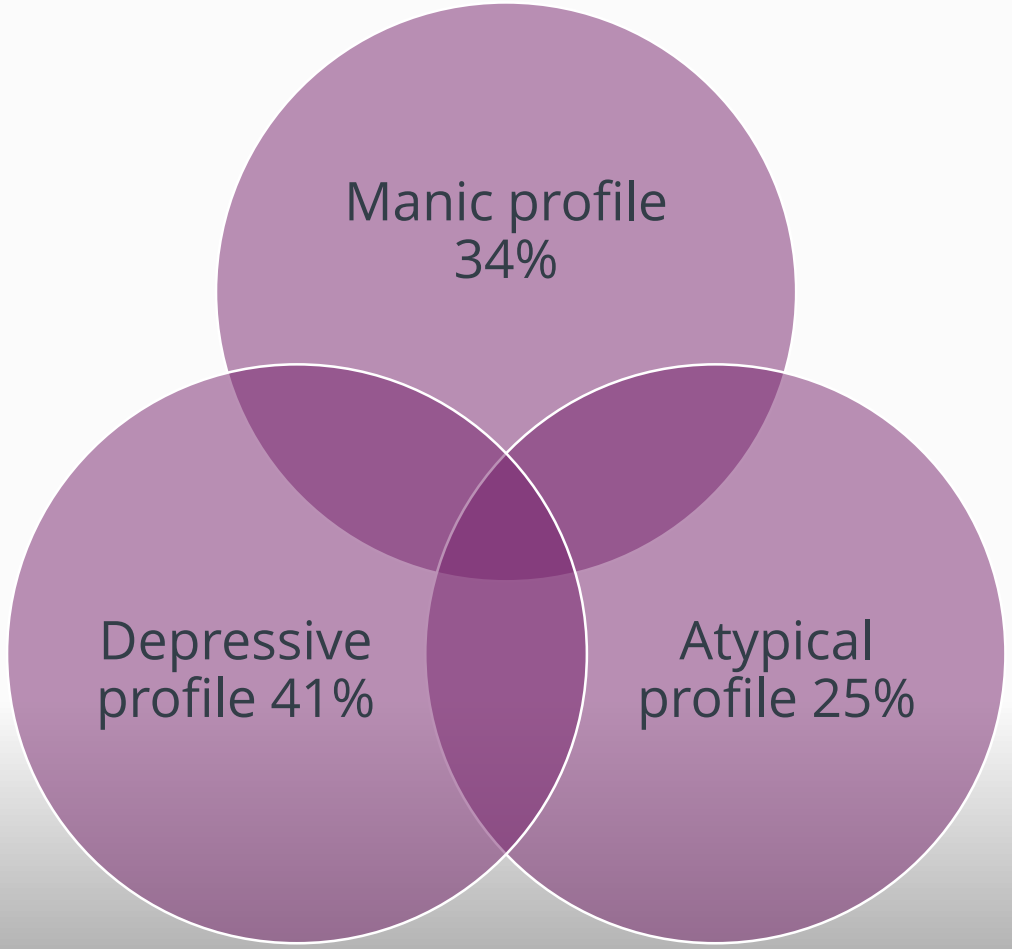
Prevalence and Differential diagnosis

- Pregnancy
  - **Relapse in pregnancy: continued meds – 37%; discontinued meds – 86%**
- Postpartum:
  - **One in two risk of any mood episode**
  - **First episode of Bipolar Disorder in 28-57%**
- Differential diagnosis
  - **Bipolar depression vs unipolar depression : 20% of women with postpartum positive depression screens actually have bipolar disorder**
  - **Bipolar Disorder and Postpartum Psychosis**

Jones, 2005

Postpartum psychosis – a heterogeneous disorder





Kamperman et al, 2017

Risk – Risk Assessment

Untreated Bipolar Disorder

- Risk of relapse
- Suicide
- Comorbidities
- Antepartum hemorrhage, placental abnormalities and C section
- PTB, LBW
- Microcephaly
- Neonatal hypoglycemia

Mood Stabilizers / Antipsychotics

- SGA / LGA
- Congenital malformations
- Neurodevelopmental outcomes

Boden 2012

Measurement-based care of bipolar disorder

- 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**

Cerimele et al, 2019

Is in utero exposure to lithium associated with Ebstein's anomaly?

Lithium during pregnancy

- ?Increased risk of Ebstein's anomaly
- No significant difference in major cardiac malformations 2.1% (0.5%-3.7%) vs 1.6% (1.0%-2.1%).
- Higher odds of any congenital anomaly (N=23,300, prevalence=4.1%, OR =1.81, 95% CI=1.35–2.41; NNH=33, 95% CI=22–77)
- Higher odds of cardiac anomalies (N=1,348,475, prevalence=1.2%, OR=1.86, 95% CI=1.16–2.96; NNH=71, 95% CI=48–167).
- 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])
- No adverse neurodevelopmental outcomes

Monk-Olsen et al, 2018; Fornaro et al, 2019

Comparing risks

- Mothers with serum lithium levels <0.64 mEq/L and dosages <600 mg/day had more reactive newborns without an increased risk of cardiac malformations.
- More effective than no lithium in preventing PP relapse (N=48, OR=0.16, 95% CI=0.03–0.89; NNT =3, 95% CI=1–12).
- Prevalence of
  - **4.2% for any malformation**
  - **1.2% for cardiac malformations**
  - **20%–70% for postpartum relapse of mood episode**

Fornaro et al, 2019

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

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. No cases of oral cleft
- 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

Mood Stabilizers during pregnancy

Mood Stabilizer	Dose / day	Rate of congenital malformation	Neurodevelopmental outcomes (no: of studies)
Valproate	<700 mg	5.6%	Poor cognitive abilities (10)
	700 – 1500	10.4%	
	≥ 1500	24.2%	
Carbamazepine	< 400 mg	3.4%	
	400 - 1000	5.3%	
	≥ 1000	8.7%	
Oxcarbazepine		2.4 - 3%	Increased risk of autism (1)
Lamotrigine	< 300 mg	2.0%	
	≥ 300	4.5%	

Antipsychotics

Antipsychotic	Congenital malformations	Pregnancy complications	Infant outcomes
Haloperidol	No increase (Approx. 200 exposures)	-	+ PTB, LBW
Perphenazine	No increase (Approx. 300 exposures)	-	No difference in mortality and BW
Quetiapine	No increase (> 5000 exposures)	No increase in risk of ~~miscarriage~~ Increase risk of GDM (RR1.28 CI 1.01-1.62)	Neonatal syndrome
Aripiprazole	No increase (> 2000 exposures)	Increase in HTN (15.4% vs 3.7%) no increase in pre eclampsia/ GDM	Increase in PTB and SGA Neonatal syndrome
Risperidone	Increase in cardiac malformations (RR 1.26 CI 0.88-1.81)	No increase in risk of GDM	Neonatal syndrome
Olanzapine	No increase (> 4000 exposures)	Increase risk of GDM	No increase in PTB or miscarriage. Neonatal syndrome
Ziprasidone	No increase (> 700 exposures)	No increase in risk of GDM	Neonatal syndrome

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	+

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

Non medication interventions

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

Take home points

- Untreated Bipolar Disorder is associated with risks for the mother and baby
- Counsel re smoking, nutritional intake and prenatal care
- 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

References

- Bergink, V., Bouvy, P. F., Vervoort, J. S., Koorengevel, K. M., Steegers, E. A., & Kushner, S. A. (2012). Prevention of postpartum psychosis and mania in women at high risk. *American Journal of Psychiatry*, *169*(6), 609-615.
- Bodén, R., Lundgren, M., Brandt, L., Reutfors, J., Andersen, M., & Kieler, H. (2012). Risks of adverse pregnancy and birth outcomes in women treated or not treated with mood stabilisers for bipolar disorder: population based cohort study. *bmj*, *345*, e7085.
- Cerimele, J. M., Goldberg, S. B., Miller, C. J., Gabrielson, S. W., & Fortney, J. C. (2019). Systematic Review of Symptom Assessment Measures for Use in Measurement-Based Care of Bipolar Disorders. *Psychiatric Services*, *70*(5), 396-408.
- Clark, C. T., & Wisner, K. L. (2018). Treatment of Peripartum bipolar disorder. *Obstetrics and Gynecology Clinics*, *45*(3), 403-417.
- Fornaro, M., Maritan, E., Ferranti, R., Zaninotto, L., Miola, A., Anastasia, A., ... & Serretti, A. (2019). Lithium Exposure During Pregnancy and the Postpartum Period: A Systematic Review and Meta-Analysis of Safety and Efficacy Outcomes. *American Journal of Psychiatry*, appi-ajp.
- Jones, I., & Craddock, N. (2005). Bipolar disorder and childbirth: the importance of recognising risk. *The British Journal of Psychiatry*, *186*(6), 453-454.
- Kamperman, A. M., Veldman-Hoek, M. J., Wesseloo, R., Robertson Blackmore, E., & Bergink, V. (2017). Phenotypical characteristics of postpartum psychosis: A clinical cohort study. *Bipolar disorders*, *19*(6), 450-457.
- Munk-Olsen, T., Liu, X., Viktorin, A., Brown, H. K., Di Florio, A., D'Onofrio, B. M., ... & Larsson, H. (2018). Maternal and infant outcomes associated with lithium use in pregnancy: an international collaborative meta-analysis of six cohort studies. *The Lancet Psychiatry*, *5*(8), 644-652.
- Thomson, M., & Sharma, V. (2018). Weighing the risks: the management of bipolar disorder during pregnancy. *Current psychiatry reports*, *20*(3), 20.
- Yatham, L. N., Kennedy, S. H., Parikh, S. V., Schaffer, A., Bond, D. J., Frey, B. N., ... & Alda, M. (2018). Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. *Bipolar disorders*, *20*(2), 97-170.

Questions/contact information

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