Postpartum Depression: It’s not just the blues

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Overview

- Etiology
- Epidemiology
- Diagnosis
- Screening
- Treatment
- Prevention
- Future Directions
Overview

- Under-diagnosed
- Unrecognized and untreated postpartum depression
  - Recurrent and persistent depression
  - Behavioral problems
  - Cognitive delays
- Affects more women than preterm labor or preeclampsia
- There is a paucity of evidence on the identification and management of PPD
Postpartum Blues

- “Baby Blues”
- 50-85% of women
- Sadness, anxiety, insomnia, and tearfulness
- Usually mild and does not interfere with functioning
Postpartum Blues

- Self limited
- Onset within first few days
- Lasting less than 2 weeks
- Treatment
  - Supportive
  - Monitor for progression or persistence
Postpartum Psychosis

- 1.1 to 4 cases per 1000 deliveries
- Acute onset, within 1st 2 weeks
- Risk factors
  - Family history bipolar or schizoaffective disorder
  - Severe, debilitating psychiatric emergency
Postpartum Psychosis

- Symptoms
  - Manic component
    - Insomnia, agitation, irritable mood, & avoidance of the infant
  - Delusions
  - Hallucinations

- Treatment
  - Neuroleptics & Mood Stabilizers
  - Inpatient Treatment
PPD Etiology

- 3 Major Theories of Depression
  - Neurotransmitter
  - Endocrine
  - Electrophysiologic

- Do not include the psychosocial influences:
  Dependency, Personality, Role changes, PP changes, etc.
1. Neurotransmitter Theory
   - Certain levels of amines and/or receptor sensitivity maintains normal mood
   - Depletion of amines (or decreased synthesis or storage) results in depression
   - The catch...
     - TCA’s affect many receptor systems
     - TCA’s main mechanism may be regulation of the receptor sensitivity
     - Newer drugs with antidepressant properties do not affect these transmitter systems (ie. carbamazepine)
2. Endocrine Theory

- NIMH study –
  - Estrogen and progesterone changes may be involved in the development of PPD
  - Women with a history of PPD are differentially sensitive

- Studies in Major Depressive Disorder suggest pituitary or hypothalamic dysfunction

- Elevated cortical steroids
- In women with PPD and thyroid disease. Both the thyroid disease and postpartum depression need to be treated

Failure to suppress cortisol

Aberrant TSH response

Diminished response of PRL, GH, CRF, melatonin

PPD Etiology

3. Electrophysiologic Theory

- Electrophysiologic studies have focused on changes in sleep function and light exposure
  - Shortened REM sleep has been shown to occur in periods of acute illness
  - Seasonal depression related to decreased exposure to light
  - These changes have been correlated with alterations in melatonin metabolism
PPD Epidemiology

Postpartum Depression

- Incidence - 14.5% of women have major or minor depression during 3 months postpartum (6.5% major)
- 0-6% identified by providers
- Risk factors
  - History of anxiety or depression
    - Prior PPD – rates 24-50%
  - Limited social support
  - Significant life events
  - Poor marital relationship
  - Other psychopathology
- Prevalence estimates for perinatal depression were not significantly different compared to appropriately matched controls, but in the 1st 5 weeks PP the odds of MDD episode or 3-fold higher

Postpartum Depression in Utah

PRAMS data 2000

- 24.1%* of women reported that they were moderately or very depressed in the months after delivery

When results weighted to represent all live births in UT (2000), an estimated 11,416 women reported being moderately or very depressed

Gaynes AHRQ Evidence Report 2005; Feregerson; Morris-Rush; Evins; Cox British J Psychiatry 1993
Postpartum Depression (PPD) Diagnosis

- Major depression with postpartum onset
  5 of the following:
  - Depressed mood*
  - Decreased interest or pleasure*
  - Appetite disturbance
  - Sleep Disturbance
  - Physical agitation or psychomotor slowing
  - Fatigue, decreased energy
  - Feeling of worthlessness or excess guilt
  - Decreased concentration or inability to make decisions
  - Recurrent thought of death or suicidal ideation

* 1 of these must be present
PPD Diagnosis

- Symptoms must be present nearly every day for 2 weeks and begin within 4 weeks of delivery
- Some epidemiologic studies use 3 months from delivery to define PPD
- Untreated PPD can last up to 6 months
- Differential Diagnosis:
  - Substance and/or medication induced mood disorders, manic episodes with irritable mood or mixed episodes, adjustment disorders, bereavement, and rarely mood disorders secondary to general medical conditions.
PPD Screening

- Nearly 50% of PPD is missed with Routine Prenatal Care
- Many scales not specific to the puerperum
  - Many normal changes overlap with somatic symptoms used to diagnose depression
    - changes in sleep patterns
    - decreased energy & libido
- Screening tests are now better at identifying PPD
PPD Screening

- Why should we screen?
  - We have interventions that decrease disease severity and duration and improve pediatric outcomes
  - Women may not be able or willing to recognize her depression
    - May view symptoms as normal
    - Fear being “bad mother”
    - Fear not meeting expectations
    - Fears baby taken away
  - BUT...There are no studies designed to directly compare screening vs. no screening and patient outcomes
PPD Screening

- Postpartum Specific Screening Scales
  - Edinburgh Postnatal Depression Screen (EPDS)
  - Postpartum Depression Screening Scale (PDSS)
Edinburgh Postnatal Depression Scale

- Developed by Cox et al. 1987
- 10 multiple choice questions
  - 30 point maximum
- Validity and reliability confirmed in multiple countries and languages

<table>
<thead>
<tr>
<th>Test Parameters</th>
<th></th>
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<tbody>
<tr>
<td>(Using a score of 12-13 as cut-off)</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>86%</td>
</tr>
<tr>
<td>Specificity</td>
<td>78%</td>
</tr>
<tr>
<td>Positive Predictive</td>
<td>73%</td>
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</table>
Edinburgh Postnatal Depression Scale

Questions 1-3

<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I have been able to laugh and see the funny side.</td>
<td>0 As much as I always could</td>
</tr>
<tr>
<td></td>
<td>1 Not quite so much now</td>
</tr>
<tr>
<td></td>
<td>2 Not so much now</td>
</tr>
<tr>
<td></td>
<td>3 Not at all</td>
</tr>
<tr>
<td>2. I have looked forward with enjoyment to things.</td>
<td>0 As much as I ever did</td>
</tr>
<tr>
<td></td>
<td>1 Somewhat less than I used to</td>
</tr>
<tr>
<td></td>
<td>2 A lot less than I used to</td>
</tr>
<tr>
<td></td>
<td>3 Hardly at all</td>
</tr>
<tr>
<td>3. I have blamed myself unnecessarily when things went wrong.</td>
<td>0 No, not at all</td>
</tr>
<tr>
<td></td>
<td>1 Hardly ever</td>
</tr>
<tr>
<td></td>
<td>2 Yes, sometimes</td>
</tr>
<tr>
<td></td>
<td>3 Yes, very often</td>
</tr>
</tbody>
</table>
Postpartum Depression Screening Scale

- Beck and Gagle
- Preliminary studies suggest improves specificity
  - 94% of women with disease correctly identified
  - Compared to 78% using the EPDS and 56% Beck Depression Inventory
- Additional validation by researchers and clinicians (other than the authors)
Screening vs. Diagnosis

- **Screening** measures are useful for the busy practitioner to alert them to those at risk.

- **Diagnosis** of PPD is by made by patient interview based on DSM-IV criteria.

- Complaints of sadness and depressed mood are not sufficient to institute pharmacologic treatment.
  - Although psychological interventions may be useful and without side effects.
PPD Treatment

- Evaluate for suicidal/homicidal ideation or plan
  - Emergent psychiatric referral

- Modalities
  - Cognitive Behavioral Therapy
  - Interpersonal Therapy
  - Pharmacologic Therapy
    - Limited number of randomized controlled trials
Cognitive Behavioral Therapy

Study Design
- 859 women screened for PPD using EPDS cut-off of 9
- 258 +screen randomized to CBT group and control arm
- CBT
  - Educational component: regarding parenting realities and guidance for infant problems
  - Supportive component: empathic listening, encouragement, and acknowledgement of maternal ambivalence
  - Cognitive Behavioral component: to weaken the “shoulds” of being a perfect mother and to develop problem solving

Reduction in depressive symptoms with 5-8 home visits

Chabrol et al. Psychol Med, 2002
Interpersonal Psychotherapy

- Brief, highly structured manual based psychotherapy addresses interpersonal issues and intervenes in the following areas of social functioning:
  - Interpersonal disputes
  - Interpersonal deficits
  - Role Transitions
  - Grief
Interpersonal Psychotherapy

- **Study Design**
  - 120 women with DSM IV diagnosed PPD
  - Randomized to 12 weeks IPT vs. control arm
- After 12 weeks, IPT patients decreased depressive symptoms in 40% compared to 13% of controls
- Unfortunately ½ declined participation, 20% dropped out

O’ Hara et al. Arch Gen Psychiatry, 2000
General Supportive Care

- Delineate appropriate activities and priorities
- Prescribe adequate:
  - Exercise
  - Diet
  - Rest
  - Health Measures
  - Family/friend support

- Medications
  - Start at half the usual initiation dose and increase slowly to decrease side effect profile
  - Responses to medications may take 4-8 weeks
  - Maintain on therapy for 6 months after remission
  - Co-manage with psychiatry and psychology
  - All ADs can be in breast milk and no long term neurodevelopmental studies exist
Pharmacotherapy

- Tricyclic Antidepressants
- Serotonin Specific Reuptake Inhibitor (SSRI)
  Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)
- Transdermal Estrogen
Tricyclic Antidepressants

- Commonly used prior to SSRI’s and in women with a previous successful response
- But, studies in PPD are limited to 2 prevention trials...
Tricyclic Antidepressants

- Side effects: sedation, weight gain, dry mouth, constipation, and hypotension

- Amitriptyline or nortriptyline
  - More sedating
  - Good for patients with insomnia or marked vegetative symptoms

- Imipramine (desipramine)
  - Less sedating

- Check CBC and LFT’s prior to initiation
TCAs and Lactation

- **Amytriptyline/Nortriptyline**
  - Unlikely to develop significant neonatal blood levels
  - Reported doses range from 0-2% of maternal concentration
  - Clinical signs were not identified

- **Desipramine**
  - No measurable amounts in neonatal blood
  - AAP – effects on the infant are unknown

Weissman et al. Am J Psychiatry 2004
Serotonin Specific Reuptake Inhibitors

- Fluoxetine (Prozac), Paroxetine (Paxil) and Sertraline (Zoloft)
- No anticholinergic side effects
- Side effects
  - General - agitation, nausea, weight gain & sexual dysfunction
  - Fluoxetine – drowsiness, anorexia & anxiety
  - Paroxetine – fatigue & dizziness
  - Sertraline – loose stool, tremor & insomnia
- May interfere with cytochrome p450 enzyme system
Serotonin Specific Reuptake Inhibitors

- 87 women
  - SSRI/1 CBT
  - SSRI/6 CBT
  - Placebo/1 CBT
  - Placebo/6 CBT

- Fluoxetine was better than placebo
- 6 CBT better than 1 CBT
- Combining Fluoxetine with 6 CBT did not improve outcome

Appleby et al. BMJ 1997
SSRIs and Lactation

- **Paroxetine & Sertraline**
  - Unlikely to develop significant plasma levels
  - Paroxetine adverse effects
    - Lethargy, poor weight gain and hypotonia

- **Fluoxetine**
  - Exposed infants were at increased risk of achieving elevated levels
  - Fluoxetine adverse effects:
    - Crying, irritability, poor feeding and GI disturbances

Weissman et al. Am J Psychiatry 2004
Transdermal Estrogen

- Two conflicting studies in the literature
  - 29 women with h/o bipolar or SAD
    - 3 transdermal dose regimens of 17 $\beta$ estradiol on PPD #2 – 14
    - No difference in PPD rates
  - 61 women with PPD diagnosis
    - Randomized to 200mcg transdermal 17 $\beta$ estradiol x 6m,
    - Last 3 months progesterone was added
    - EPDS used to compare rate of improvement
    - Greater extent of and faster improvement of PPD symptoms

- Decreased milk production and increased risk of thromboembolism may limit utility

Kumar et al.; Gregoire Lancet 1996
Prevention

- Not a benefit to psychosocial interventions in primary prevention in all women
  - Including home visits, group counseling...
- May be benefit to targeting at risk women, using professionally-based postpartum care
- Medications for secondary prevention (at risk)
  - Nortriptyline – 2 studies,
    - open trial suggested a benefit (62.7 vs. 6.7%)
    - RCT did not
  - Sertraline – only one study
    - Conferred a significant reduction
    - Limited by sample size

<table>
<thead>
<tr>
<th>PPD development</th>
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<tbody>
<tr>
<td>Sertraline</td>
<td>1/14</td>
</tr>
<tr>
<td></td>
<td>(7%)</td>
</tr>
<tr>
<td>Placebo</td>
<td>4/8</td>
</tr>
<tr>
<td></td>
<td>(50%)</td>
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</table>
Further data are needed...

Are the prevalence and incidence of PPD different across racial and ethnic lines?

What is the mechanism of disease?

Are the rates of perinatal depression greater than the general population?

Effectiveness and cost effectiveness of screening?

Timing of screening and disease occurrence?

Additional Risk Factors?
Coming Soon to Salt Lake City...
The Association of Obesity and Postpartum Depression

- Correlations suggest link between Obesity and PPD

- Hypothesis
  - There is an association between maternal obesity and PPD
  - Risk of PPD increases with BMI
  - Unique RF's for PPD in obese women
## PRAMS Study

*Maternal Depressive Symptoms Stratified by Severity and Prepregnancy BMI category*

<table>
<thead>
<tr>
<th>Depressive Symptoms</th>
<th>Underweight</th>
<th>Normal</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;= Moderate</td>
<td>n 4,714</td>
<td>11,047</td>
<td>2,342</td>
<td>4,280</td>
</tr>
<tr>
<td></td>
<td>weighted n 27.7%</td>
<td>22.8%</td>
<td>24.8%</td>
<td>30.8%</td>
</tr>
<tr>
<td></td>
<td>+/-2.2</td>
<td>+/- 1.2</td>
<td>+/- 2.9</td>
<td>+/- 2.5</td>
</tr>
<tr>
<td>&lt;= Little</td>
<td>n 12,289</td>
<td>37,442</td>
<td>7,113</td>
<td>9,639</td>
</tr>
<tr>
<td></td>
<td>weighted n 368</td>
<td>368</td>
<td>368</td>
<td>368</td>
</tr>
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PPD and Obesity Study

FIGURE 2: Patient Tracking - Flow Diagram
PPD in Utah

![Bar chart showing the percentage of PPD in Utah based on emotional and traumatic stressors.]
PPD in Utah

- **Risk Factors**
  - Young, unmarried, < high school, low SES, unintended pregnancy, history of abuse, limited social support
Preliminary Analysis - PRAMS
Maternal BMI and Postpartum Depressive Symptoms

- PRAMS
  (Pregnancy Risk Assessment Monitoring System)
- CDC sponsored, 31 states
- Random population-based survey of maternal attitudes and experiences
Preliminary Analysis - PRAMS
Maternal BMI and Postpartum Depressive Symptoms

- Utah Data from 2000-2001
- “In the months after your delivery, would you say that you were...
  Not depressed at all, Moderately depressed, Very depressed, Very depressed and had to get help?”
- Responses were stratified by prepregnancy BMI
- Analyzed using SUDAAN
Preliminary Analysis - PRAMS
Maternal BMI and Postpartum Depressive Symptoms

<table>
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<tr>
<th></th>
<th>Underwt</th>
<th>Normal</th>
<th>Overwt</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\geq$ moderate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$sample\ n$</td>
<td>196</td>
<td>445</td>
<td>95</td>
<td>184</td>
</tr>
<tr>
<td>$weighted\ n$</td>
<td>4714</td>
<td>11047</td>
<td>2342</td>
<td>4280</td>
</tr>
<tr>
<td>$%$</td>
<td>27.7%</td>
<td>22.8%</td>
<td>24.8%</td>
<td>30.8%</td>
</tr>
<tr>
<td>$s.e.$</td>
<td>+/-2.2</td>
<td>+/- 1.2</td>
<td>+/- 2.9</td>
<td>+/- 2.5</td>
</tr>
<tr>
<td>$\leq$ little</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$sample\ n$</td>
<td>520</td>
<td>1361</td>
<td>270</td>
<td>368</td>
</tr>
<tr>
<td>$weighted\ n$</td>
<td>12289</td>
<td>37442</td>
<td>7113</td>
<td>9639</td>
</tr>
</tbody>
</table>
Preliminary Analysis - PRAMS
Maternal BMI and Postpartum Depressive Symptoms

- After controlling for marital status and income, pre-pregnancy Overweight and Obesity was a risk factor for PP depressive symptoms (aOR 1.5; CI 1.2-2.0)

- Extremes of BMI associated with depressive symptoms

- Correlation of PPD with eating disorders already established, the association between BMI and PPD warrants further investigation
PPD and maternal obesity

- Prospective design with oversampling
- Quantify the relationship between BMI and PPD
  - 2 large urban hospitals in Salt Lake City, UT
- Identify potential social, psychological, medical, and/or obstetrical RF in the obese and non-obese
PPD Screening

- Edinburgh Postnatal Depression Scale
  - Widely validated
  - PPV 73%

- Body Shape Questionnaire
  - Valid & reliable instrument of patient concern regarding body size and shape
Study Design

- 1653 women
- Inclusion Criteria
  - Singleton
  - >37 weeks
  - live births
- Stratified into 3 groups
  - Normal weight at Delivery (BMI 19-29.9)
  - Class I Obesity at Delivery (BMI 30-34.9)
  - Class II & III Obesity at Delivery (BMI >35)
Study Design

- **Data Collection**
  - Ht, Wt @ 1\textsuperscript{st} and last PNV
  - Patient data
    - demographics
    - medical
    - psychiatric hx
    - family hx
    - obstetric outcomes
    - patient-provider discussion history
Study Design

- **Outcome Measures**
  - 8 week PP EPDS & BSQ mailed to patient
  - Primary Outcome Measure = EPDS > 12
    - Sensitivity 85-86%
  - Risk factors for obese vs. non-obese

- **Safety Net**
FIGURE 1: Directed Acyclic Graph of Delivery BMI and PPD
Light Therapy

- Antepartum