



## **Infertility and Perinatal Loss**

### **Epidemiology of Perinatal Loss and Comorbid Psychiatric Conditions** *Self-Study*

#### **Contributors**

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#### **Session Overview**

- 1) Review pre-reading
- 2) Using the data presented and pre-reading content, develop answers for the discussion questions presented
- 3) Review references for further study

#### **Learning Objectives**

At the conclusion of this self-directed study activity, learners will be able to:

- 1) Describe the epidemiology of early and late pregnancy loss
- 2) Identify the common pre-morbid and post-morbid psychiatric complications associated with perinatal loss
- 3) Describe the risk of suicide in women who have experienced perinatal loss

#### **Recommended reading to accompany the self-study guide (complete list of references below):**

Maconochie N, Doyle P, Prior S, Simmons R. Risk factors for first-trimester miscarriage—results from a UK-population-based case-control study. *BJOG* 2007;114:170–186.

Gold KJ, Dalton VK, Schwenk TL, Hayward RA. What causes pregnancy loss? Preexisting mental illness as an independent risk factor. *General Hospital Psychiatry* 2007;29:207-213.

Hunter A, Tussis L, MacBeth A. The presence of anxiety, depression, and stress in women and their partners during pregnancies following perinatal loss: A meta-analysis. *Journal of Affective Disorders* 2017;223:153-164.

Hvidtjørn D, Wu C, Schendel D, Thorlund Parner E, Brink Henriksen T. Mortality in mothers after perinatal loss: a population- based follow-up study. *BJOG* 2016;.123:393–398.



## Case Vignette 1a

*As a reproductive psychiatry consultant at an obstetric hospital, you are called to evaluate a patient recently admitted for management of pregnancy loss at 21 weeks' gestation. The obstetric team is concerned about the woman's risk of depression.*

*Maria is a 27-year-old unmarried Hispanic woman, G3P1021, with a previous history of miscarriage at seven weeks' gestation and full-term birth of her 3-year-old son. She denies depressive symptoms during this current pregnancy but reports increased anxiety during the first trimester due to her previous pregnancy loss. On her evaluation, Maria presents as tearful and withdrawn. She denies current suicidal ideation.*

- 1) What can you tell Maria and her partner about perinatal loss? How do you answer her questions about why this happened to her?
- 2) How do you define perinatal loss? What is the frequency, and what are the most common etiologies of perinatal loss?

### Epidemiology of perinatal loss:

- **Definition**
  - **Perinatal loss:** non-voluntary end of pregnancy or death of a baby from conception until 28 days postpartum (Bhat & Byatt 2016)
    - Spontaneous abortion or Miscarriage
      - before 20 weeks, as defined in the US
    - Intrauterine Fetal Demise (IUFD) or Stillbirth
      - after 20 weeks or after reaching 14 ounces in weight
    - Early (<7 days) or late (7-28 days) neonatal death
    - Termination for fetal abnormalities or genetic indications
  - **Recurrent perinatal loss:** 3 or more losses (the classic definition), but has more recently been redefined by the American Society of Reproductive Medicine (ASRM) as two or more losses
- **Frequency**
  - 10-15% of pregnancies end in loss before 20 weeks
    - 75% of losses occur before 12 weeks of gestation
  - Stillbirth after 20 weeks affects 1% of all births
  - Many early first trimester losses may never be recognized as pregnancy (this may be as common as in 1/3 of all pregnancies)
  - 50-80% of women who have experienced perinatal loss will get pregnant again
- **Common etiology**
  - Chromosomal abnormalities
  - Fetal anomalies
  - Death of fetus during labor and delivery
  - Preterm labor
  - Hypertensive disorders



- Umbilical cord abnormalities
- Infection
- Other medical conditions, including thyroid abnormalities, diabetes
- Unknown causes: 50% of cases

- **Presentation**

- Miscarriage typically presents as vaginal bleeding and pain and is confirmed by ultrasound.
- Later pregnancy loss may present as a woman no longer feeling her fetus move or identified by ultrasound at a routine visit

3) What risk factors for perinatal loss can you identify for Maria? What are other common risk factors?

**Risk factors for perinatal loss**

- Increased maternal age
- History of prior miscarriage
- Infertility
- Thrombophilias
- Parental cytogenetic abnormalities
- More controversial: social and lifestyle factors
  - Alcohol use
  - Smoking
  - Caffeine intake
  - Stress and emotional well-being
- Recurrent perinatal loss

**Management of perinatal loss**

- Expectant management
- Medical and surgical interventions
- For stillbirth: allowing parents to hold infant, memory boxes
- Common grief reactions

**Case Vignette 1b**

*After obtaining further history, Maria has disclosed to you that she has a previous history of depression with onset in adolescence and past postpartum depression following the birth of her son. She has been in and out of treatment in the past and has been prescribed an SSRI, which was effective for her symptoms.*

*In addition to assessing her current mental status, what are the factors to consider in assessing her risk of future mental health exacerbation and the contribution of her past mental health history to her current presentation?*

1) What types of psychiatric co-morbidities are associated with an increased risk of perinatal loss? Was this patient at greater risk of miscarriage based on her psychiatric history?

## **Psychiatric Co-morbidities PRIOR to perinatal loss:**

- Does maternal mental illness increase the risk of pregnancy loss?
    - Women with pre-pregnancy mental health disorders are more likely to have pregnancy loss (unadjusted OR 1.36 CI 1.07-1.74 and adjusted OR 1.8 CI 1.35-2.41) (Gold et al, 2007)
    - Affective and substance use disorders were significant risk factors for loss, but not anxiety disorders (Gold et al, 2007)
    - Hypothesis as to etiology includes the effect of depression and other mental illnesses on the HPA axis and sympathetic nervous system
      - Stress activates the HPA axis
      - Triggers adrenocorticotrophic hormone, corticotropin-releasing hormone, and maternal glucocorticoids
      - Can promote the release of placental prostaglandins, increase the effect of oxytocin on the uterus, and up-regulate pro-inflammatory cytokines
        - All have implications for preterm labor
      - Other factors likely include decreased prenatal care in women with active mental illness, decreased physical activity, and likely other unidentified or unmeasured risks
    - Maternal mental illness has been linked to an increased risk of both infant mortality and SIDS (Gentile 2008)
  - Does psychotropic medication (specifically SSRI) use increase the risk of perinatal loss?
    - Some studies have identified an increased risk of stillbirth/miscarriage with the use of SSRIs in pregnancy, but studies that control for maternal characteristics and severity of underlying mental illness (typically depression) no longer find a significant association (Stephansson et al. 2013)
    - Women with a history of perinatal loss that leads to depression are often reluctant to take antidepressant medication out of concern that the medication will increase the risk of subsequent pregnancy loss
    - As described above, depression itself is a risk for perinatal loss
- 2) Does perinatal loss increase the risk of psychiatric comorbidities, either immediately after or in the future?

## **Psychiatric Comorbidities AFTER Perinatal Loss:**

- **Bereavement**
  - Higher risk of persistent complex bereavement disorder (formerly “complicated grief disorder”) than with other types of loss, especially in the setting of:
    - Poor psychosocial support
    - Premorbid MDD
    - Ambivalence about pregnancy
    - Termination of pregnancy for fetal anomaly
  - The presence of older children is protective against complicated grief



- **Depression & anxiety**

- Risk factors for depression after miscarriage include (Bhat & Byatt 2016):
  - Highest risk for intrauterine fetal demise or pregnancy loss after 20 weeks of gestation
  - Infertility treatment
  - Recurrent pregnancy loss
  - Prior history of depression
  - Prior PTSD
  - Intimate partner violence
  - High levels of distress immediately following a miscarriage
- Perceived low levels of support increase the risk of depression in subsequent pregnancy and the postpartum period
- Pregnancy within a year following a loss also increases the risk of depression and anxiety in a subsequent pregnancy
- In women with multiple losses, the risk of depressive and anxiety symptoms increases with each subsequent loss (Blackmore et al., 2011)

- **Mania**

- Case reports in the literature that it may be similar in etiology to postpartum psychosis.
- More commonly reported in patients with a history of bipolar disorder
- Etiology may be related to the fluctuation in estrogen levels with the end of pregnancy

3) What are the risks of mental illness during a future pregnancy following a perinatal loss?

- Increased risk of depression and anxiety in subsequent pregnancies and even following delivery of a healthy child
  - Depression and anxiety following loss do not resolve after the birth of a healthy child
  - The impact lasts well past a future healthy pregnancy
  - Parents report decreased attachment to the baby in pregnancies subsequent to perinatal loss (Armstrong & Hutti 1998)
  - Implications for the role of perinatal loss as a risk factor for perinatal depression
    - Important to screen at-risk populations
- A meta-analysis (Hunter et al., 2017) showed an association between perinatal loss and depression and anxiety in subsequent pregnancies, which has been replicated by multiple other studies
  - Type of perinatal loss did not affect women's anxiety levels or increase stress during subsequent pregnancies but did affect depression levels (miscarriage did not increase risk, but stillbirth and combined loss types did)
  - A previous perinatal loss increased pregnancy-specific/state anxiety more so than trait anxiety



- Fathers showed increased anxiety in subsequent pregnancies following perinatal loss
- Other areas of impact include attachment, PTSD, number of living children, and time between perinatal loss and future pregnancy addressed in other studies
  - Mothers with high levels of depression in a subsequent pregnancy describe concern about their level of investment in their infants
  - 50% of women have another pregnancy within one year of perinatal loss (stillbirth specifically)

4) What is the risk of developing PTSD after perinatal loss?

- PTSD
  - Lifetime prevalence of PTSD of 29% following a stillbirth and 21% in the third trimester of a subsequent pregnancy
  - Greater gestational age at the time of loss is correlated with greater severity of PTSD
  - Risk factors include:
    - Young age
    - Lower education level
    - Previous trauma
    - History of past mental illness

### Case Vignette 1c

*You evaluate this patient, Maria, in your outpatient clinic approximately three weeks after her hospital discharge. At that time, the patient presented with worsening depressed mood, anhedonia, decreased sleep, nightmares about her experience of delivering the fetus in the hospital, and difficulty spending time with her older child. She will not initially answer questions about suicidality. However, her partner reports that she has made several concerning statements at home about not wishing to be alive anymore or wishing to join her deceased child. You are concerned about the patient's safety and her risk of suicide following her loss.*

### Discussion Questions

- 1) Is suicide a risk of perinatal loss? Under what circumstances?
- 2) What are the protective factors against suicide following perinatal loss?

### **Suicide risk/Maternal mortality after loss:**

- Several studies show an increase in the risk of traumatic death/suicide after the loss of a child, particularly immediately following the loss
  - The mean annual suicide rate in the first year following a miscarriage is 18.1 out of 100,000, compared to 5.9 out of 100,000 following live birth (Hvidtjørn et al 2016, Bhat & Byatt 2016)
- Mothers who lose a child describe ambivalence about their own mortality
- Suicide can serve multiple purposes:
  - Release from the pain of loss
  - Reunion with the deceased child
- Obligations to other children can be a protective factor, particularly for the mother



## References and Further Reading

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