Hypertensive Disease of Pregnancy: Recurrence Risk and Prevention

Lauren Theilen, M.D.

Maternal-Fetal Medicine Fellow

University of Utah Health Sciences Center

Case

- 30 yo G1 P0101 presents to clinic for her 6 week postpartum visit.
- Preeclampsia with severe features diagnosed at 27 weeks, delivered at 29 weeks.
- Blood pressure today is normal, and she has not required antihypertensives since delivery.
- No other medical problems.

Case

- “If I get pregnant in the future, what are the chances that I’ll have preeclampsia?”
- “What can I do to keep from getting preeclampsia in a future pregnancy?”

Hypertensive disease of pregnancy

Available in a Variety of Flavors!

Gestational Hypertension

Preeclampsia without Severe Features

Preeclampsia with Severe Features

HELLP Syndrome

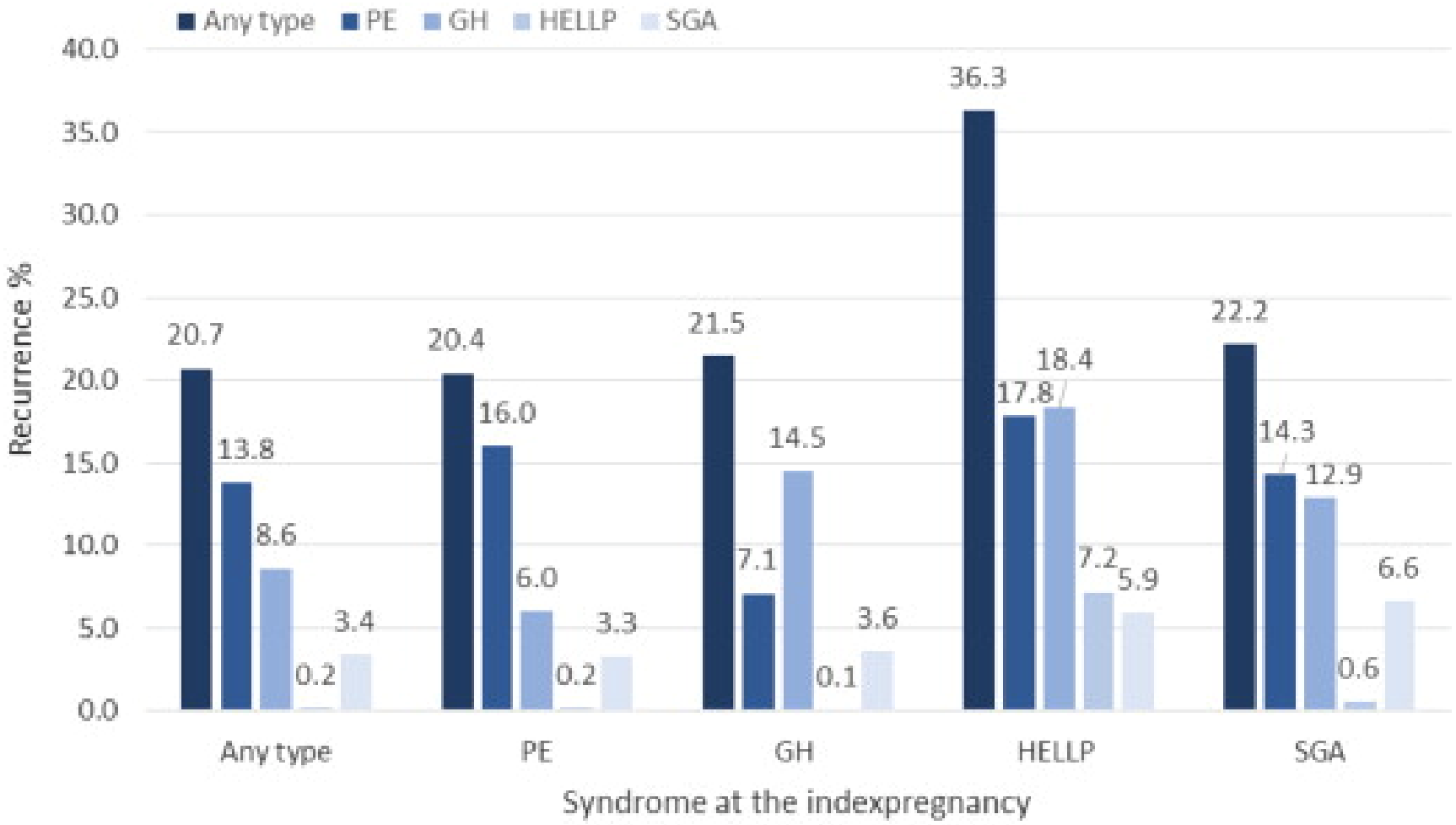
Eclampsia

Recurrence risk overall

- Recent meta-analysis of individual patient data from 22 studies
- 99,415 women with a pregnancy complicated by a hypertensive disorder of pregnancy who had a subsequent pregnancy
  - 20,545 had a recurrent hypertensive disorder of pregnancy (20.7%, 95% CI 20.4-20.9)

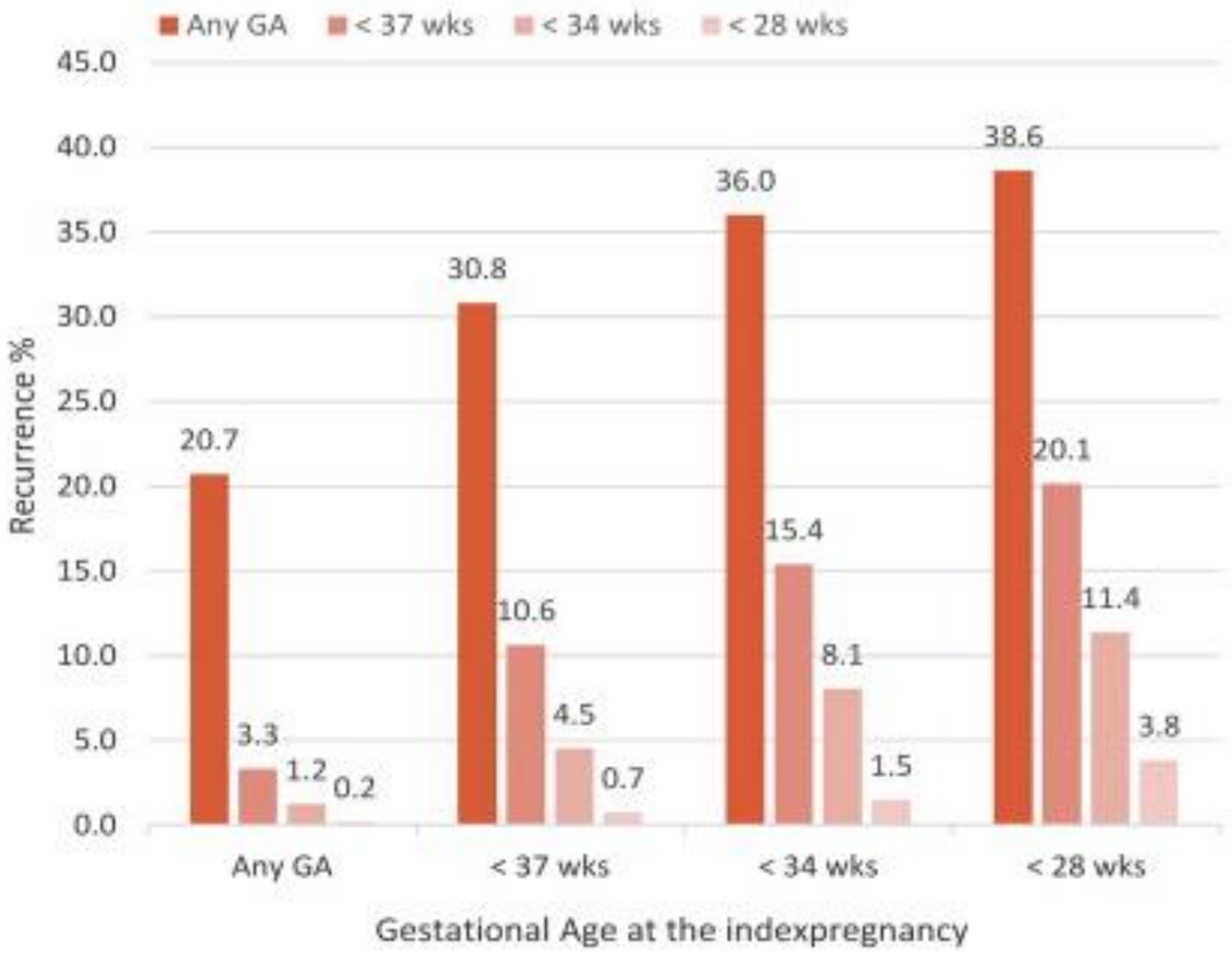
van Oostward MF et al. AJOG 2015.

Recurrence risk based on type of disease



van Oostward MF et al. AJOG 2015.

Recurrence risk based on gestational age



van Oostward MF et al. AJOG 2015.

Predictors of recurrent preeclampsia

- History of preeclampsia and any of the following:
  - HELLP syndrome
  - Delivery of SGA neonate
  - Preterm at the time of diagnosis
  - BMI >30 kg/m^2
  - Chronic hypertension

van Oostward MF et al. Pregnancy Hypertens 2014.
van Oostward MF et al. AJOG 2015.

Predictors of primary preeclampsia

- No history of preeclampsia and any of the following:
  - Pregestational diabetes
  - Chronic hypertension
  - Renal disease
  - Autoimmune disease
  - Multifetal gestation

WHO 2011.
LeFevre ML for USPSTF. Ann Intern Med 2014.

Prevention

- Activity reduction
  - Cochrane review of 2 small RCTs including 106 normotensive women at moderate risk of developing preeclampsia
    - Significant reduction in risk of preeclampsia
      - Imprecise proxy outcomes
      - Very small sample size
      - Scarce data
- Not recommended

Meher S, Duley L. Cochrane Database Syst Rev 2006.
WHO 2011.

Prevention

- Dietary salt restriction
  - Cochrane review of 2 RCTs including 603 nulliparous normotensive women in the Netherlands
    - Compared restricted dietary salt (20-50 mmol/day) with advice to continue normal diet
    - No significant differences in preeclampsia, perinatal death, admission to intensive care unit, or 5-minute Apgar score less than 7
- Not recommended

Duley L, Henderson-Smart D, Meher S. Cochrane Database Syst Rev 2005.
WHO 2011.

Prevention

- Calcium supplementation
  - Cochrane review of 13 RCTs including 15,730 women supplemented with 1.5-2 g calcium/day
    - 96.2% of women had a low risk for developing preeclampsia
    - Over 70% had low baseline dietary calcium (<900 mg/day)
    - 64% risk reduction for preeclampsia in 8 trials involving populations with low baseline dietary intake
    - No statistically significant reduction in risk of preeclampsia in 4 trials involving populations with adequate dietary calcium intake
- Recommended in areas where dietary calcium intake is low

Hofmeyr GJ et al. Cochrane Database Syst Rev 2010.
WHO 2011.

Prevention

- Vitamin D supplementation
  - One RCT including 400 women randomized to 1200 IU vitamin D with 375 mg elemental calcium/day compared to no supplementation
    - No difference in risk of preeclampsia
- Not recommended

De Regil LM et al. Cochrane Database Syst Rev 2011.
WHO 2011.

Prevention

- Antioxidants
  - Cochrane review of 15 RCTs including 22,359 women
    - Most trials compared combined vitamins C and E regimens to placebo
    - No statistically significant differences maternal or neonatal outcomes, even when considering various risk levels for developing preeclampsia and gestational age at study entry
- Not recommended

Rumbold A et al. Cochrane Database Syst Rev 2008.
WHO 2011.

Prevention

- Antiplatelet agents
  - Cochrane review of 60 RCTs involving 37,720 pregnant women at moderate to high risk for developing preeclampsia
    - Aspirin compared with placebo or no treatment
    - Statistically significant difference in risk of preeclampsia was consistent across risk groups although more marked among high risk women (RR 0.86, 95% CI 0.76-0.89 vs RR 0.75, 95% CI 0.66-0.85)
- Recommended
  - Low-dose aspirin (75 mg/day) initiated after 12 weeks gestation but before 20 weeks gestation in women at high risk for preeclampsia

Duley L et al. Cochrane Database Syst Rev 2007.
WHO 2011.
LeFevre ML for USPSTF. Ann Intern Med 2014.

Prevention

- Heparin
  - In addition to antithrombotic effect, unfractionated and LMWH promote in vitro angiogenesis in placental tissue
  - Cochrane review of 9 studies including 979 women at risk of placental dysfunction (history of preeclampsia/eclampsia, renal disease, abruption, IUGR, or IUFD)
    - Compared heparin +/- dipyridamole or aspirin to no treatment
      - No significant difference in risk of preeclampsia or eclampsia
- Not recommended

Sobel ML et al. Obstet Gynecol 2011.
Dodd JM et al. Cochrane Database Syst Rev 2013.

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Case

- Recurrence risk?
- Prevention strategy?

Summary

- Overall recurrence risk for hypertensive disease of pregnancy is 20.7%
- Women with a history of HELLP syndrome or with a history of hypertensive disease of pregnancy diagnosed before 34 weeks gestation have a recurrence risk nearing 40%
- Low-dose aspirin should be offered starting at 12-20 weeks gestation for women at high risk of developing preeclampsia
  - This includes women with no prior history of hypertensive disease of pregnancy!