Preeclampsia – A Rural Health Crisis

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Educational Objectives

- Understand the prevalence of preeclampsia (PET) and gestational hypertension (GHTN) in rural compared to urban communities
- Diagnosis, evaluation and treatment of PET and GHTN
- Current challenges in diagnosing and treating PET and GHTN

Disclosure

- Site PI Azalea study, Jannsen Pharmaceuticals, Johnson & Johnson (ongoing)
- Site PI Freesia study, Jannsen Pharmaceuticals, Johnson & Johnson (about to begin)
- Site PI CHAPS Study, NICHD

Prevalence of PET/GHTN

- Prevalence has been increasing over the past few decades

- 1990 5.0% nationally
- 2020 8.2% nationally
- 2023 10.3% nationally - 15% in Oregon

Oregon Center for Health Statistics, 2023

National Vital Statistics Report 2025

DeSisto CL, et al Hypertension at delivery hospitalization—United States, 2016-2017. *Pregnancy Hypertens*. 2021;26:65-68

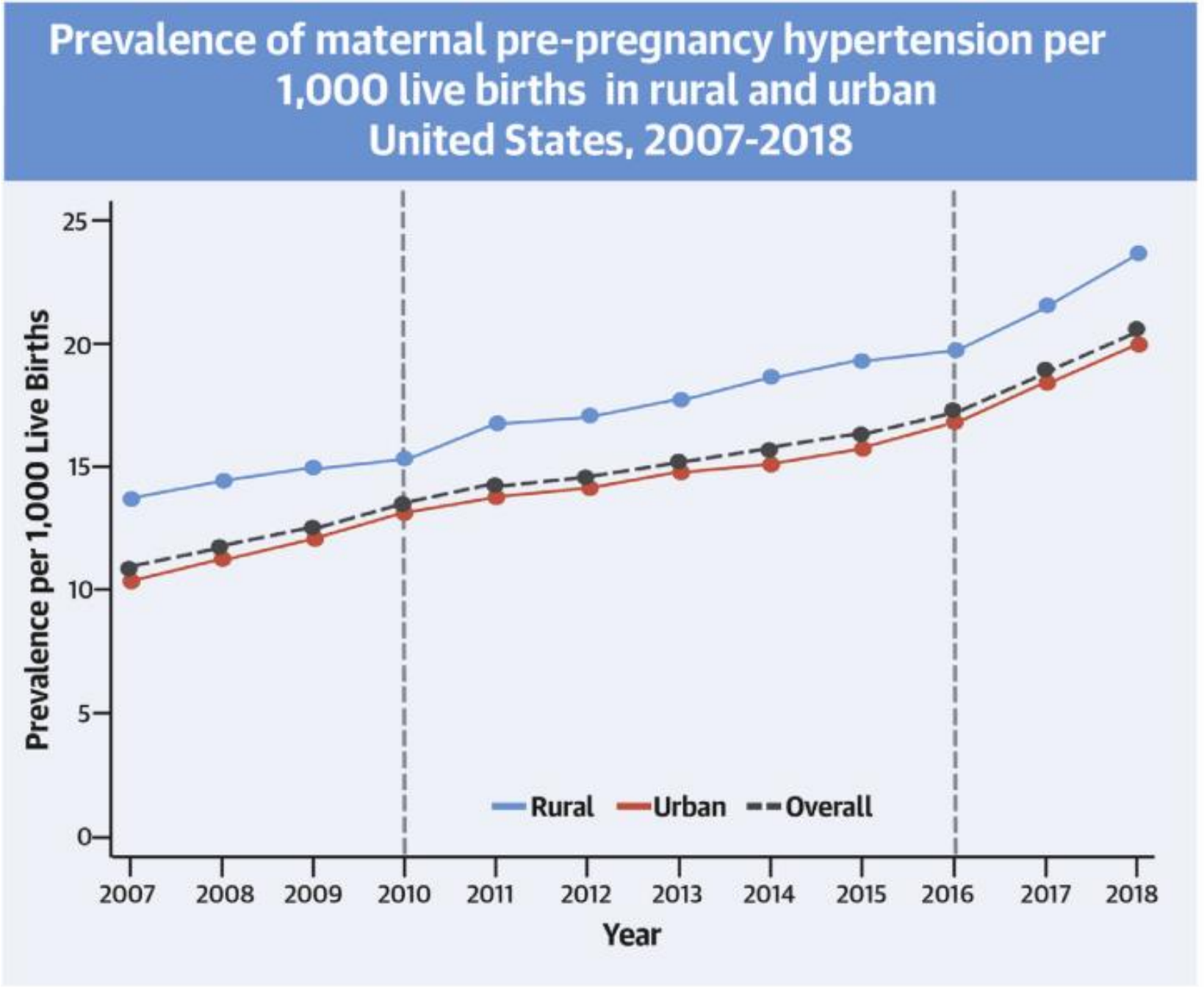
Bruno AM, et al. Trends in Hypertensive Disorders of Pregnancy in the U.S 1989 to 2020, *Obstet Gynecol*, 2022; 1:14091)83-86

Prevalence of PET/GHTN

- Pre-pregnancy hypertension is higher in rural compared to urban communities nationally:

Year	Rural	Urban
2007	13.7%	10.5%
2018	23.7%	20.0%

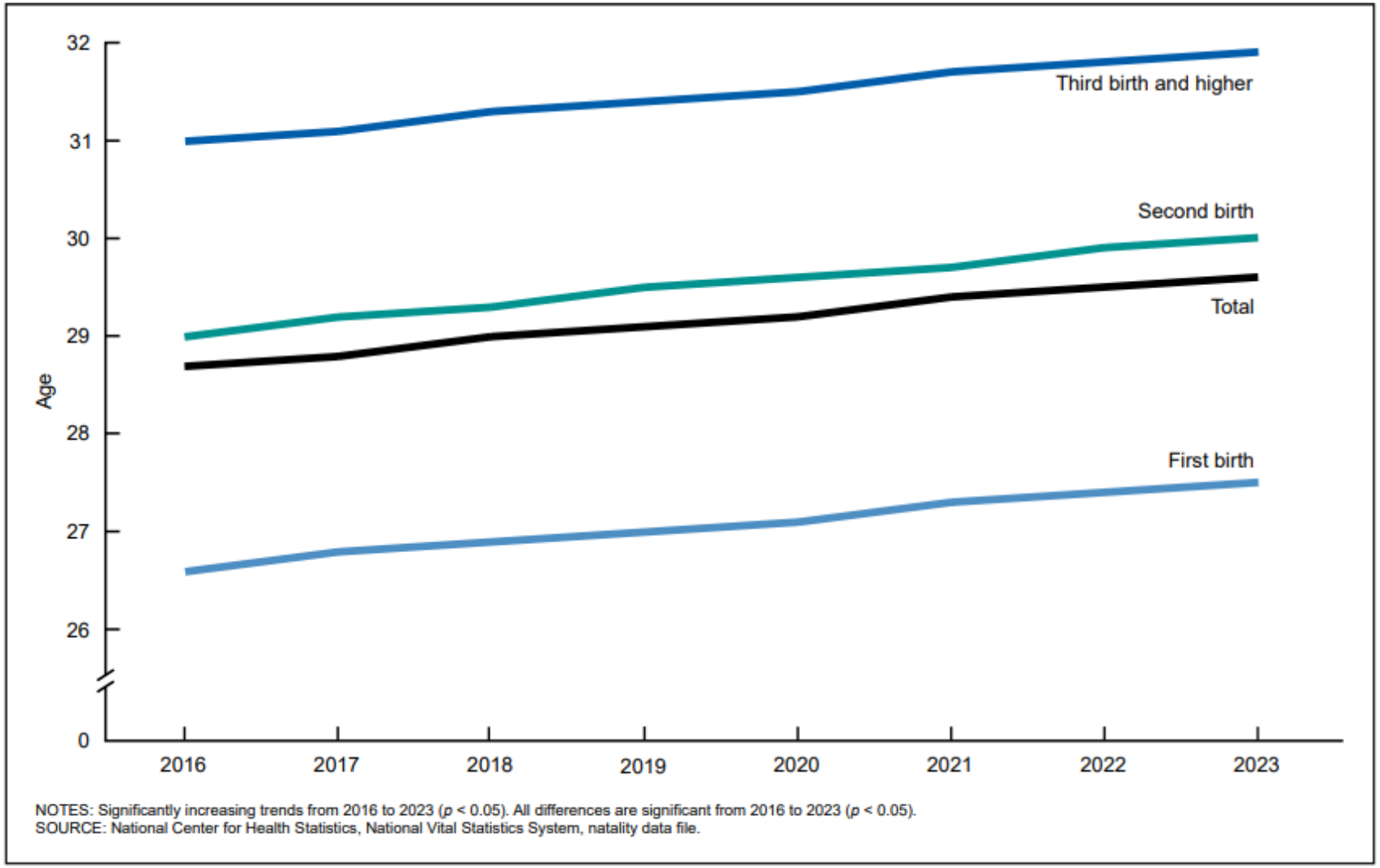
Cameron NA, et al. Pre-pregnancy Hypertension Among Women in Rural and Urban Areas of the United States. *J Am Coll Cardiol*. 2020 Nov 9;76(22):2611–2619.



Cameron NA, et al. Pre-pregnancy Hypertension Among Women in Rural and Urban Areas of the U.S. *J Am Coll Cardiol*. 2020 Nov 9;76(22):2611-19.

Pre-pregnancy age is increasing nationally

Figure 1. Mean age, by birth order: United States, 2016–2023

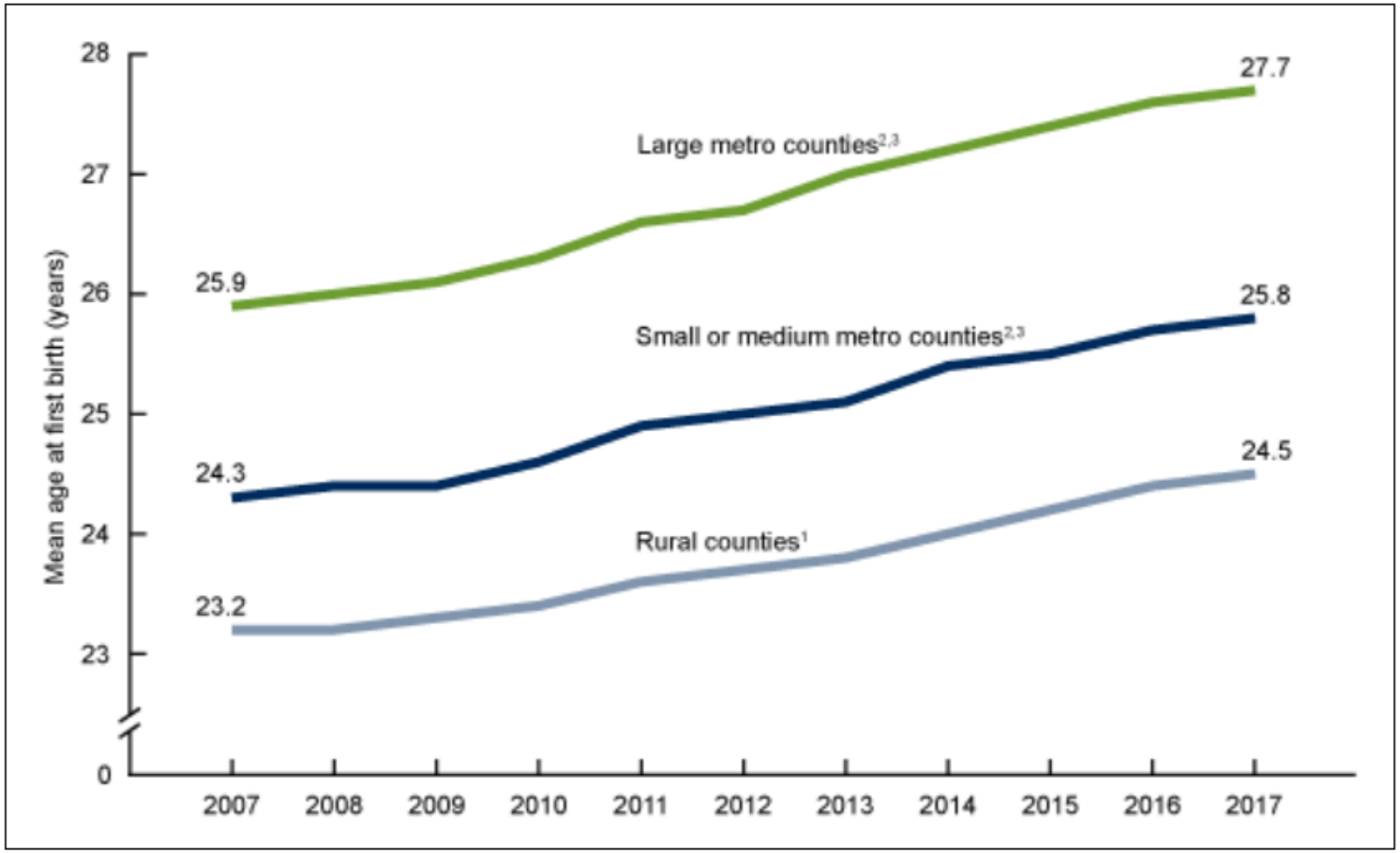


NOTES: Significantly increasing trends from 2016 to 2023 ($p < 0.05$). All differences are significant from 2016 to 2023 ($p < 0.05$).
SOURCE: National Center for Health Statistics, National Vital Statistics System, natality data file.

National Vital Statistics Report 74(9) June 13, 2025

Pre-pregnancy age is increasing in rural areas

Figure 3. Mean age at first birth, by urbanization level: United States, 2007–2017



Trends in Fertility and Mother's Age at First Birth Among Rural and Metropolitan Counties: United States, 2007–2017, NCHS Data Brief ,323, 2018

Prevalence of PET/GHTN

- Pre-pregnancy BMI is increasing nationally:

Year	BMI > 30 (%)
2016	26.1%
2019	29.0%
2023	32.0%

NCSH Data Brief 2020
National Vital Statistics Repor-2025

DRAFT -Prevalence of PET/GHTN

- Pre-pregnancy BMI is higher in rural compared to urban communities nationally:

Year	Rural	Urban
South Carolina 2006	30.7%	25.8%
Minnesota 2019	33.0%	26.6%
Oregon 2019	27.4%	24.8%

Gallagher A, et al. Maternal Obesity and GWG in Rural versus Urban Dwelling Area in South Carolina. *J of Rural Health*. 29, 2013; 9-11.

Emery Tavernier RL, et al. Trends in Maternal Weight disparities: Statewide Differences in Rural and Urban Minnesota Residents From 2016 to 2019. *Women's Health Issues.* 2023, 33 (6); 636-42.

Radin JM, et al. Pregnancy health in POWERMOM participants living in rural versus urban zip codes. J Clin Transl Sci 2020, 4(5);457-62.

Significance of the high prevalence of PET/GHTN in rural communities

- Higher rates of morbidity and mortality - women in rural areas die at a higher rate from pregnancy-related complications compared with women in urban areas
- The rural-urban gap in severe maternal morbidity and mortality is projected to continue to grow
- Limited access to health care may render rural women particularly vulnerable to experience adverse maternal outcomes
- The rural-urban gap may be more pronounced among certain racial and ethnic groups, further amplifying known disparities by race/ethnicity in maternal HTN

Kozhimannil KB, et al. Rural-urban differences in severe maternal morbidity and mortality in the US, 2007–15. *Health Aff (Millwood)* 2019;38:2077–85.

Diagnosis, Evaluation and Treatment of PET/GHTN

GHTN: NEW-ONSET HTN

- usually after 20 weeks
- BP $\geq$ 140/90 in a previously normotensive patient on 2 occasions at least 4 hours apart
- sustained elevation, sitting position
- severe HTN 160/110 mmHg for more than 15 minutes
- SBP or DBP

Diagnosis, Evaluation and Treatment of PET/GHTN

PREECLAMPSIA: GHTN with one of the following

- Either proteinuria $\geq$ 300 mg/24h, P:C ratio $\geq$ 0.3 or $\geq$ 2+ on a clean catch urinalysis in a patient without underlying nephropathy and no urinary tract infection

- or one of the following

  thrombocytopenia < 100,000 10^9/L

  renal insufficiency: Cr > 1.1 mg/dL or doubling in the absence of renal disease

  AST or ALT 2x normal

  pulmonary edema

  new onset headache – unresponsive to medication and not accounted for by alternative diagnoses or visual symptoms

Diagnosis, Evaluation and Treatment of PET/GHTN

PREECLAMPSIA WITH SEVERE FEATURES

- BP $\geq$ 160/110 on 2 occasions at least 4 hours apart (unless antihypertensive therapy is initiated before 4 hrs)

- or BP $\geq$ 140/90 in a previously normotensive patient on 2 occasions at least 4 hrs apart *AND one of the following*

  - Thrombocytopenia < 100,000 10^9/L
  - Impaired liver function not accounted for by alternative diagnosis: - AST or ALT 2x normal
  - Severe, persistent right upper quadrant/epigastric pain unresponsive to medications
  - Renal insufficiency: Cr > 1.1 mg/dL or doubling in the absence of renal disease
  - Pulmonary edema
  - New onset headache unresponsive to medication and not accounted for by alternative diagnoses
  - Visual disturbances (diploplia, scotomata)

Diagnosis, Evaluation and Treatment of PET/GHTN

PREECLAMPSIA SUPERIMPOSED UPON CHTN:

Occurs in a patient with CHTN (hypertension that precedes pregnancy or is present on at least two occasions before the 20th week of gestation or persists longer than 12 weeks postpartum) with *either*:

- worsening or resistant hypertension (especially acutely)
- new onset of proteinuria or a sudden increase in proteinuria
- significant new end-organ dysfunction after 20 weeks of gestation or postpartum

HELLP (Hemolysis, Elevated Liver Enzymes, and Low Platelet Count) SYNDROME:

- Hemolysis – LDH > 600 IU/L
- AST and ALT > 2x normal
- Platelets < 100 10^9/L

Diagnosis, Evaluation and Treatment of PET/GHTN

GHTN

- Expectant management until 37 0/7 weeks

PREECLAMPSIA WITHOUT SEVERE FEATURES

- Expectant management until 37 0/7 weeks

- Administration of antenatal steroids before 37 0/7 weeks
- May be managed as an outpatient (twice weekly fetal monitoring, weekly labs, growth scans q 3-4 weeks
- FGR with normal Dopplers, AFI, and FHR monitoring
- Delivery does not mean Cesarean
- Consider $MgSO_4$ for seizure prophylaxis (controversial)

Diagnosis, Evaluation and Treatment of PET/GHTN

PREECLAMPSIA WITH SEVERE FEATURES

Immediate delivery indicated*

- Administer MgSO4 for seizure prophylaxis
- Do not wait for steroids if > 34 0/7 weeks
- Individualize delivery plan (induction versus CS, consider setting a timetable if attempting TOL)
-Regional anesthesia acceptable with PLT > 70 10^9/L

*Expectant management may be appropriate in certain situations

Current challenges

- Early Detection of PET
- Use of LD ASA
- Diagnosis and Detection in Rural Areas
- Use of Magnesium Sulfate
- Delivery Timing

Early Detection of PET

- First trimester PAPP-A, PlGF, uterine artery PI Doppler has a good sensitivity for early onset preeclampsia (93% sensitivity, with a 5% FP rate), but not for term preeclampsia (38% sensitivity)

- Second/third trimester – high sFlt-1/PlGF ratio > 85 associated with development of early onset preeclampsia (<34 weeks) sensitivity of 88%, NPV 99.5%

- After 34 weeks, sFlt-1/PlGF ratio > 110 was associated with preeclampsia sensitivity 58%, NPV 95.5%

Kornacki J et al. Utility of biochemical tests in prediction, diagnostics and clinical management of preeclampsia: a review. *Arch Med Sci*. 2020; 16(6): 1370-5.

Early Detection of PET

- Although several studies have evaluated these biomarkers, their PPV remains low overall at 8-33 %; no single test reliably predicts preeclampsia and further prospective investigation is required to demonstrate clinical utility

- At this time, the use of biomarkers and ultrasonography to predict preeclampsia and should remain investigational.

Kornacki J et al. Utility of biochemical tests in prediction, diagnostics and clinical management of preeclampsia: a review. *Arch Med Sci*. 2020; 16(6): 1370-5.

Use of LD ASA

- Meta-analysis: 9 trials in patients with CHTN to reduce superimposed preeclampsia
  - no net benefit in reduction of preeclampsia OR 0.83 (.55-1.25)
  - Reduction in preterm birth OR 0.63 (.45-.89)
  - Dose of ASA varied from 60-150 mg

- USPTF review: 23 RCTs in patients at risk for preeclampsia
  - 23 RCTs OR 08.5 (.75-.95)
  - Reduction in preterm birth OR 0.80 (.67-.95)
  - Dose of ASA varied from 50-150 mg

Richards EMF. Low-dose aspirin for the prevention of superimposed preeclampsia in women with chronic hypertension: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2023; 228(4):395-408.

Henderson JT, et al. Aspirin Use to Prevent Preeclampsia and Related Morbidity and Mortality: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA* 2021; 326 (12): 1192-1206.

Use of LD ASA

- Modest benefit – recommend in high-risk patients
- 81 – 162 mg (dose may be individualized or standard)
- Ideally start 12-16 weeks
- Less benefit if started > 20 weeks; no benefit > 28 weeks
- Who should be on it:
  - h/o preeclampsia
  - multifetal gestation
  - renal disease, autoimmune disease, type 1 or type 2 diabetes, and CHTN
  - or 2 of the following: primigravida, AMA > 35, BMI > 30, FH of preeclampsia, high risk sociodemographic characteristics and personal history factors

ACOG Committee Opinion 2018.

Diagnosis and detection in rural areas

- Challenges with access to care/distance/transportation may lead to delays in diagnosis and account for some of the increased morbidity/mortality seen in rural populations
- Telemonitoring – home blood pressure monitoring
- CRADLE 2019 - 8% reduction in primary outcome (hysterectomy, eclampsia, maternal death) 0.92 (.82-97) 79.4 per 10,000 to 72.8 per 10,000
- Point-of-care diagnostic tests – need further study

Vousdon N, et al. Effect of a novel vital sign device on maternal mortality and morbidity in low-resource settings: a pragmatic, stepped-wedge, cluster-randomised controlled trial – CRADLE trial. Lancet 2019; 7(3): 347-56.

Use of MgSO4

PREECLAMPSIA WITHOUT SEVERE FEATURES: Use of MgSO4 prophylaxis is controversial

Witlin RCT 1997: 135 patients (67 MgSO4, 68 placebo), eclampsia 0/0, progression to severe preeclampsia 12.0% vs. 9%, RR 1.4 (0.5-3.7), pp hemorrhage 6% vs 1%, RR 4.1 (0.5-35.4)

Livingston RCT 2003: 222 patients (109 Mg, 113 placebo), eclampsia 0/0, progression to severe preeclampsia 12.8 % vs. 16.8 %, RR 0.8 (0.4-1.5), pp hemorrhage 1% vs 0.9%

Cahill 2007: Decision Analytic Model: either strategy is acceptable

MgSO4 prophylaxis is recommend for patients with preeclampsia with severe features 4:2 or 4:1

Witlin AG, et al. The Effect of Magnesium Sulfate on the Duration of Labor in Women with Mild Preeclampsia at Term: A Randomized, Double-Blind, Placebo-Controlled Trial. *AJOG* 1997; 176 (3): 623-7.

Livingston JC et al. Magnesium sulfate in women with mild preeclampsia: a randomized controlled trial. *Obstet Gynecol* 2003; 101 (2) 217-20.

Cahill AG, et al. Magnesium for Seizure Prophylaxis in Patients with Mild Preeclampsia. *Obstet Gynecol* 2007; 110(3):601-7.

Delivery Timing

Expectant Management of Severe Preeclampsia < 34 weeks gestation

1. **Periviability:** 350-500 gm, 22-24 weeks' gestation

2. **Administration of antenatal steroids < 34 0/7 weeks – for 48 hours**

3. **Proteinuria > 5 gm/24h – no longer part of the criteria for severe preeclampsia;** no effect on maternal or perinatal outcome

4. **Fetal growth restriction**
- with reassuring fetal testing
- FGR fetuses will do worse than AGA at each gestation
- 80 to 90% will deliver within 1 week
- average interval from admission to delivery is 3 days

Delivery Timing

Expectant Management of Severe Preeclampsia < 34 weeks gestation

5. Severe range HTN in patients with CHTN

- antihypertensive therapy for maintenance of BP in a normal range
- **Regimens:**
  labetalol PO BID (start 100mg BID, max 2400 mg/day)
  nifedipine XL PO QD (start 30mg QD, max 120 mg/day)
  amlodipine PO QD (start 2.5 mg QD, max 10 mg/day)
  clonidine PO BID/TID (start 0.1 mg TID, max 2.4 mg/day)

- no expectant management of acute hypertensive crisis in patients presenting without a h/o CHTN – goal of treatment is to stabilize patient to prevent hemorrhagic CVA during delivery

- exception is if severe HTN due to another pathology (drug use, pain)

Delivery Timing

Expectant Management of Severe Preeclampsia < 34 weeks gestation

5. Severe range HTN in patients with CHTN

- potentially dangerous due to intravascular volume depletion may precipitate ischemia or fetal heart rate changes
- consider prior to 34 0/7 weeks
- has been shown prospectively to prolong gestation by 7 to 15 days with no increase in maternal complications
- reduction in NICU admissions, days in the NICU, intubation, RDS, and composite neonatal morbidity/mortality

6. INPATIENT and patient and fetal conditions are stable

Odendaal et al. *Obstet Gynecol* 1990.
Sibai et al. *Am J Obstet Gynecol* 1994.

Delivery Timing

Expectant Management of Severe Preeclampsia Contraindications

1. **34 0/7 WEEKS**
2. **CNS DYSFUNCTION** unresponsive to medication and not accounted for by alternative diagnoses; high risk of PRES with eclampsia
3. **LIVER HEMATOMA / RUPTURE**
4. **PULMONARY EDEMA / ARDS**
5. **CARDIAC FAILURE**
6. **RENAL FAILURE / OLIGURIA**
7. **HELLP SYNDROME**
8. **DIC**
9. **PTL**
10. **ABRUPTION**
11. **NONREASSURING FETAL TESTING**
12. **ELEVATED BLOOD PRESSURE FAILING OPTIMAL (COMBINATION) ANTIHYPERTENSIVE THERAPY**

Delivery Timing

Expectant Management of Severe Preeclampsia Goals

1. **Benefit of antenatal steroids**
2. **Gestational ages where prolongation for days to weeks may make a difference**
3. **Gain days when time is necessary to make a definitive diagnosis**
4. **Decreased perinatal morbidity**
5. **Decreased perinatal mortality**

Delivery Timing
Expectant Management of Severe Preeclampsia

1. **Management plan must be made in conjunction with patient**

2. **Patients must understand there is maternal risk to conservative management**

3. **Weigh risks (abruption, IUFD, emergent CS, worsening maternal conditions) with potential fetal benefits**

4. **Involve neonatologist in discussion**

5. **Set realistic goals (48 hrs, 7 days)**

6. **Most malpractice cases involve failure to diagnose and treat severe preeclampsia NOT due to complications from expectant management**