Cardiac Conditions of Pregnancy:

Case and Review

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UAB MEDICINE

ALABAMA PERINATAL QUALITY COLLABORATIVE
ALPQC

Objectives

1. Recognize dyspnea red flag signs and symptoms
2. Review two cases of dyspnea in pregnancy
3. Appreciate medication selection across pregnancy/postpartum continuum
4. Realize the utility of biomarkers and team-based care

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Dyspnea in Pregnancy

- Underestimating severity → inadequate investigation → maternal mortality
- French nationwide analysis from 2007-2015, 13.3% of all maternal deaths were attributable to cardiovascular disease
- Among the 23 women whose deaths were determined to be preventable – "Missed or delayed diagnosis of heart failure" in the context of acute dyspnea was the main preventability factor

C Diguisto, P-M Choinier, …C Deneux-Tharaux, et al. "Timing and Preventability of Cardiovascular-Related Maternal Death." Obstet Gynecol. 2023 Jun 1;141(6):1190-1198.

Dyspnea in Pregnancy

- Maternal mortality in Alabama = 41.4 per 100,000 births (during pregnancy or within 6 weeks after pregnancy ends)
- Maternal mortality in the U.S. = 23.5 per 100,000 births

National Center for Health Statistics, Mortality data, 2018-2021.

Dyspnea Red Flags in Pregnancy

- Thorough history!
  - Wheezing, coughing, chest tightness (asthma?)
  - CBC (anemia?)
  - Sudden onset, pleuritic, hemoptysis, desaturation with ambulation, risk factors for DVT (PE?)
  - Fever, productive cough, risk factors (pneumonia? sepsis?)
  - Orthopnea, paroxysmal nocturnal dyspnea, peripheral edema, palpitations, limitations in ADLs (heart disease?)
  - Syncope (pulmonary hypertension?)

Dyspnea Red Flags in Pregnancy

- Physical exam:
  - Vital signs (BP, HR)
  - Jugular venous distension
  - Lower extremity edema
- Objective data:
  - 6mw test
  - Biomarkers
  - 12-lead ECG
  - Echocardiogram
  - Rhythm monitor
  - Chest radiograph
  - PFTs
  - Vascular ultrasound
  - Contrast CT

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Case 1:
Peripartum cardiomyopathy

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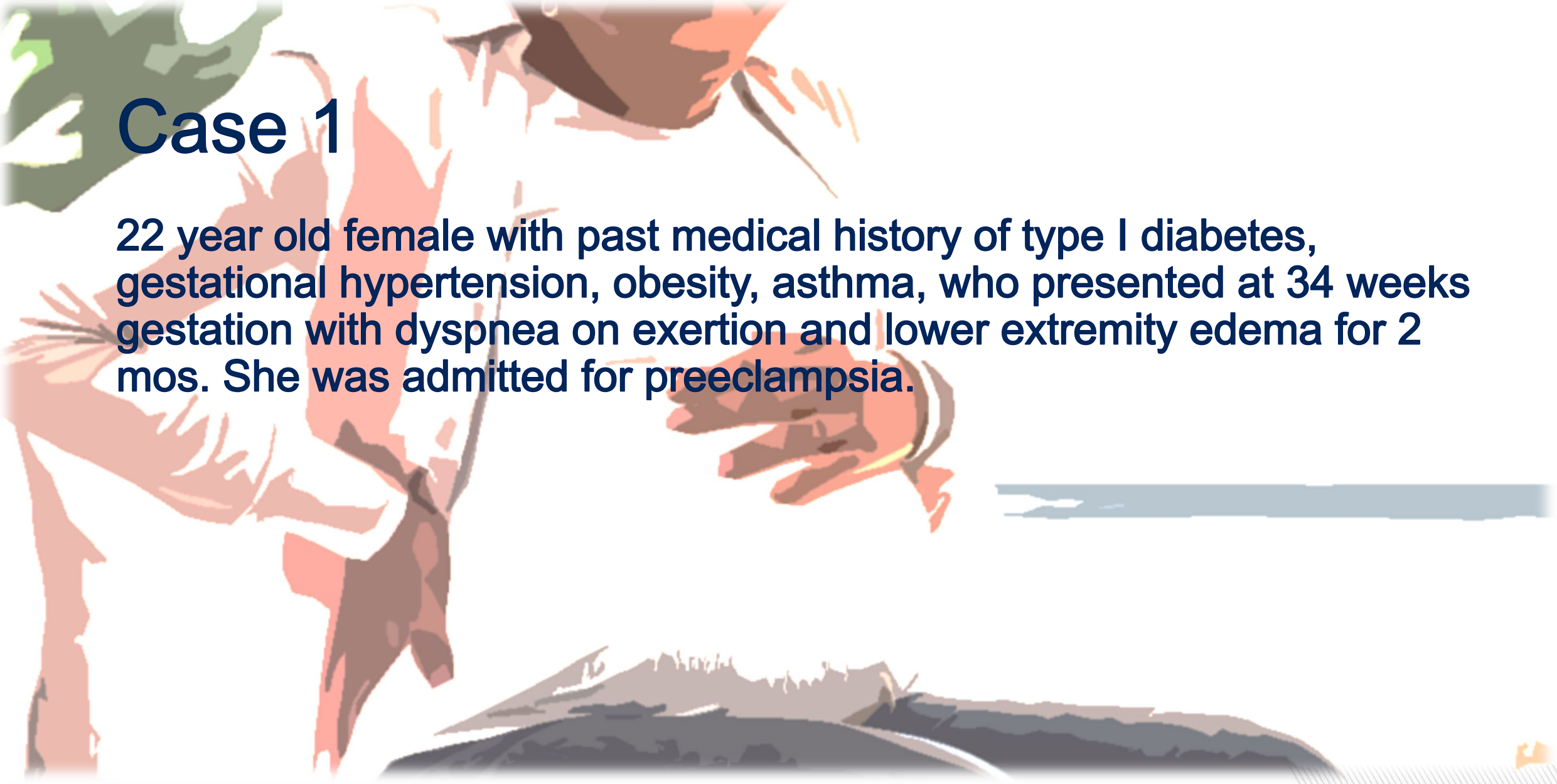
Case 1

22 year old female with past medical history of type I diabetes, gestational hypertension, obesity, asthma, who presented at 34 weeks gestation with dyspnea on exertion and lower extremity edema for 2 mos. She was admitted for preeclampsia.



Case 1

- At her local hospital, she received IV antihypertensives and magnesium
- Betamethasone was given in anticipation of early delivery
- She was transferred to UAB Labor & Delivery service for management of preeclampsia

Case 1

- On arrival, BP 156/70, HR 100; initially given nifedipine
- Labs showed anion gap metabolic acidosis with respiratory compensation and ketonuria consistent with DKA; initiated on insulin drip and given 4L IV fluids on hospital day 1
- She also had symptoms of upper respiratory infection, Rhinovirus+

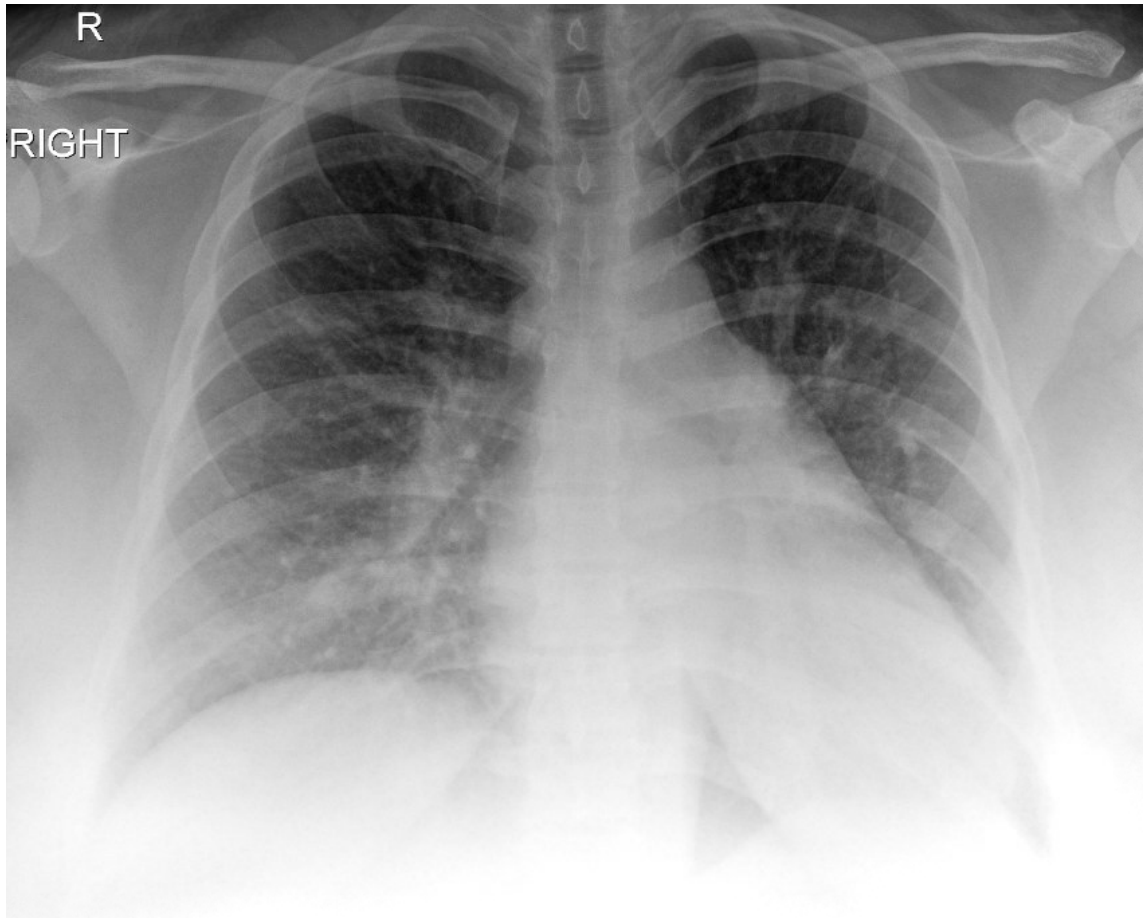
Case 1

- On hospital day 3, she developed acute respiratory distress overnight
- CXR showed pulmonary edema and BNP was 452
- She received furosemide IV and felt mildly improved

Case 1

- With echo pending, L&D team made the decision to proceed with delivery for severe preeclampsia; induction was started with oxytocin
- On hospital day 5, she had an uncomplicated vaginal delivery of a healthy but premature baby girl, planned to breastfeed
- Post-delivery echocardiogram showed LVEF 35-40% (new)

Case 1



Case 1

- Our Advanced HF team was consulted: patient was massively volume overloaded with 4+ symmetric lower extremity pitting edema up to the hips and lower abdomen
- She was visibly dyspneic and reported orthopnea, chest pain while supine
- Over the next few days we aggressively diuresed with IV furosemide
- We changed nifedipine to enalapril, added carvedilol; both were titrated to a goal SBP 100 to 120, and HR 60 to 80

Case 1

- She was finally able to sleep fully flat in bed, and edema was almost completely resolved
- She was discharged to stay locally, as her baby would need significantly more time in the Neonatal ICU

Case 1

- Close outpatient follow-up was arranged 3 days post-discharge on the reduced doses of GDMT
- Due to symptomatic hypotension in clinic, carvedilol and enalapril were discontinued, and furosemide was changed to PRN
- At the most recent follow-up, she was feeling well and euvolemic: BP 100/73, HR 93; Repeat echocardiogram is pending

Case 1 *Learning Points*

- Good choices for routine pregnant patients with hypertension:
  - Labetolol
  - Nifedipine
  - Methyldopa
- Manage blood pressure! in pregnancy and postpartum
  - Goal 130s/80s OR LESS

AT Tita et al for CHAP Trial Consortium. "Treatment for Mild Chronic Hypertension during Pregnancy." NEJM.org, April 2, 2022.

Case 1 *Learning Points*

- Pre-eclampsia and hypertensive disorders of pregnancy are significant risk factors for the development of cardiovascular disease in the future – warrants closer monitoring
- Hypertensive disorders of pregnancy connote a 4-fold increase in risk of longterm HF

SA Goldstein and NJ Pagidipati. "Hypertensive Disorders of Pregnancy and Heart Failure Risk." Curr Hypertens Rep. 2022 Mar 28.

Case 1 *Learning Points*

- Good choices for pregnant patients with HTN and LV dysfunction:
  - Metoprolol (ESC suggests carvedilol also fine)
  - Hydralazine
  - Nitrates

  *Avoid ACEi, ARB, ARNI, MRA, SGLT2i, CCBs

MB Davis, Z Arany, ...U Elkayam, et al. "Peripartum Cardiomyopathy: JACC State-of-the-Art Review." J Am Coll Cardiol. 2020 Jan 21;75(2):207-221.

Case 1 *Learning Points*

- Blood pressure, heart rate goals may be similar to non-pregnant patients with heart failure
  - Goal systolic 100-120s
  - Goal heart rate 60-100 bpm (vs. 60-80 bpm)
  - Monitor daily

  *Not enough data for ivabridine, avoid for now

MB Davis, Z Arany, ...U Elkayam, et al. "Peripartum Cardiomyopathy: JACC State-of-the-Art Review." J Am Coll Cardiol. 2020 Jan 21;75(2):207-221.

Case 1 *Learning Points*

- If LV dysfunction is present <u>while breastfeeding</u>, bring back:
  - Enalapril

  *Add back spironolactone only if maxed out of Bblocker, ACEi, or in need of K-sparing (safe. may decrease milk production)

MB Davis, Z Arany, ...U Elkayam, et al. "Peripartum Cardiomyopathy: JACC State-of-the-Art Review." J Am Coll Cardiol. 2020 Jan 21;75(2):207-221.

Case 1 *Learning Points*

- Symptomatic management throughout pregnancy and breastfeeding:
  - Loop diuretics (need to balance comfort and milk production)
  - Digoxin

MB Davis, Z Arany, ...U Elkayam, et al. "Peripartum Cardiomyopathy: JACC State-of-the-Art Review." J Am Coll Cardiol. 2020 Jan 21;75(2):207-221.

Case 1 *Learning Points*

- Close follow-up is ideal
- As physiology changes, may need to adjust doses
- Following EF with serial echos will be key to understanding future risk

Case 1 *Learning Points*

- Risk regarding subsequent pregnancy
  - Women with persistent LV dysfunction <50% have high risk of both recurrence/ deterioration of heart failure and mortality with subsequent pregnancy
  - Death rate reported to be 16-25% based on two major studies
  - Higher rates of poor fetal outcomes, such as stillbirth, pre-term delivery

Hypothesis: Risk may be less if the patient is followed carefully by a multidisciplinary, coordinated care team?

Elkayam U. Risk of subsequent pregnancy in women with a history of peripartum cardiomyopathy. J Am Coll Cardiol 2014;64:1629–36.

Hilfiker-Kleiner D, Haghikia A, Masuko D, et al. Outcome of subsequent pregnancies in patients with a history of peripartum cardiomyopathy. Eur J Heart Fail 2017;19:1723–8.

Case 1 *Learning Points*

- Risk regarding subsequent pregnancy
  - Women with improved LV function >50% have lower risk of mortality and complications, but there is still ~20% risk of recurrence of heart failure
  - Studies show mixed results, but half to all of patients who relapsed did recover

Hilfiker-Kleiner D, Haghikia A, Masuko D, et al. Outcome of subsequent pregnancies in patients with a history of peripartum cardiomyopathy. Eur J Heart Fail 2017;19:1723–8.

Codsi E, Rose CH, Blauwet LA. Subsequent pregnancy outcomes in patients with peripartum cardiomyopathy. Obstet Gynecol 2018;131:322–7.

Case 2:
Heart failure in pregnancy

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Case 2

37 year old female with past medical history of congestive heart failure due to non-ischemic cardiomyopathy with EF 30%, hypertension, type II diabetes, obesity, and a current smoker who presented to the E.D. with worsening dyspnea and edema.

Case 2

10 Weeks

- Had not followed-up with prior cardiologist, TTE confirmed EF 30%, BNP 300, BP 100/65, HR 95
- Also found to be 10 weeks pregnant
- Referred to UAB Cardio-Obstetrics clinic (including Maternal Fetal Medicine and Heart Failure)

10 Weeks

- She was counseled that continuing the pregnancy = high risk (WHO class IV by EF, NYHA class?)
- Started on low dose metoprolol and furosemide with improvement, furosemide made PRN
- She opted to continue the pregnancy; Smoking cessation was recommended

Case 2

16 Weeks

- She quit smoking and was doing better, able to do an office job and household chores
- BP 105/60, HR 82, BNP 212, EF stable at 30%, taking furosemide PRN once every 1-2 weeks

19 Weeks

- She was hospitalized briefly for volume overload, requiring IV diuretics
- Discharged on furosemide three times a week

Case 2

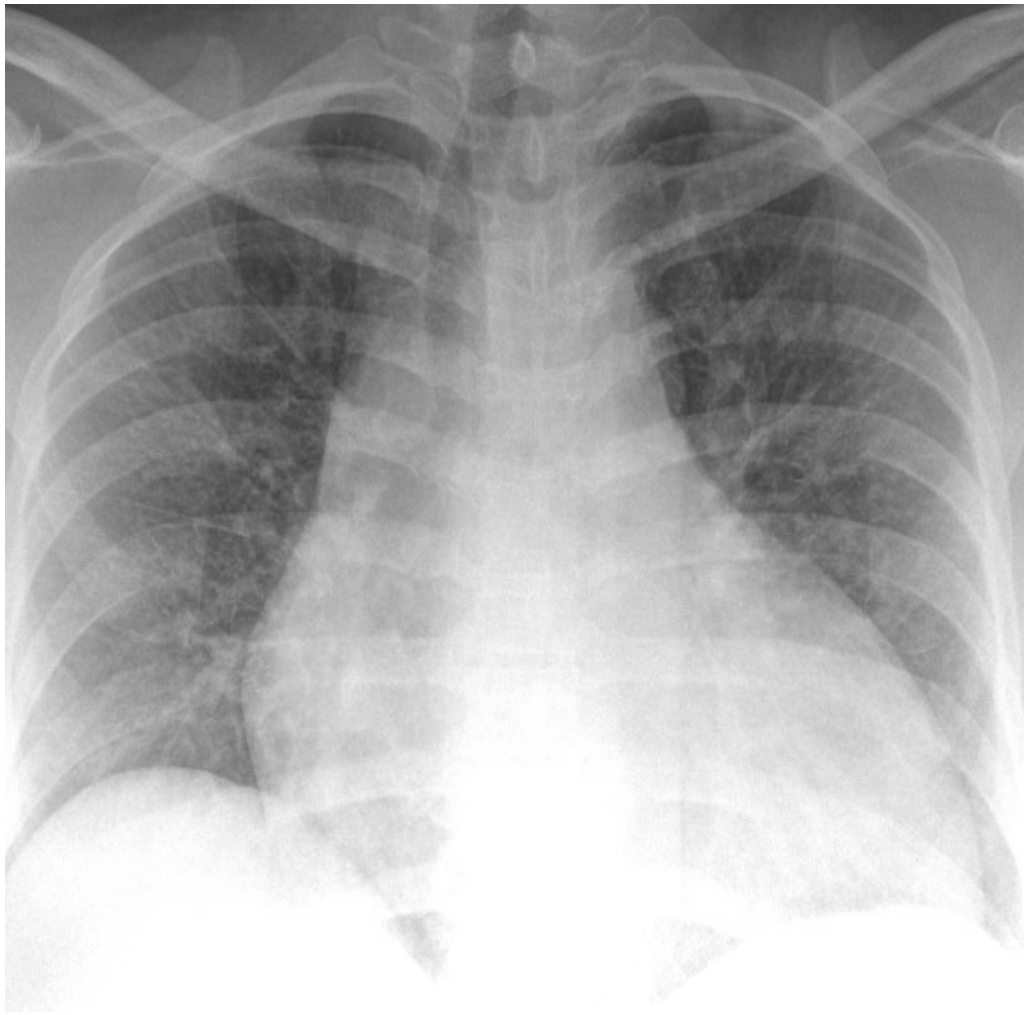
28 Weeks

- She was able to do her office job and chores, but needed to rest more often, noted new orthopnea
- BP 108/63, HR 80, EF stable at 30%
- Following with MFM and HF clinic weekly

34 Weeks

- She was visibly dyspneic and volume overloaded
- EF now ↓20-25%, BNP ↑680, AKI noted
- Multidisciplinary team meeting (MFM, HF, Anesthesia, Nursing, Pharmacy) discussed delivery plan

Case 2



Case 2

34 Weeks

- She was urgently admitted: IV diuresis, telemetry, hemodynamic optimization
- RHC safely done: RA 16, PA 56/22 (39), PW 29, PA sat 50%, Fick CI 1.9, Thermo CI 2.1, SVR 1800
- Diuresed to CVP of 12, metoprolol switched to hydralazine, BP 110/72, HR 85

35 Weeks

- Dobutamine used for inotropic support, induction attempted, but failed to progress
- She then underwent successful c-section with neuraxial anesthesia, plus tubal ligation
- Mild pulmonary edema managed with BiPAP and IV diuresis

Case 2

Postpartum

- Healthy baby boy born!
- Postpartum monitoring in CVICU, dobutamine weaned off in 2 days, despite low EF
- Mom elected not to breastfeed

Discharge

- Metoprolol restarted, tolerated well
- Stable on daily furosemide, LifeVest fitted, mother and baby discharged home

Case 2

1 Week Postpartum

- HF clinic: She was able to do ADLs, take care of her baby, no orthopnea, still losing weight
- Low dose sacubitril-valsartan started

8 Weeks Postpartum

- Repeat TTE showed EF ↑35-40%, avoiding placement of ICD
- Hydralazine stopped, spironolactone started, BNP improved
- Genetic test revealed pathogenic variant, pediatrician to arrange genetic testing for children

Case 2

- The patient continues to follow with our clinic
- We continue to manage guideline directed medical therapy, optimize at every appointment
- EF has stayed around 35-40%, but she has been well compensated, requiring no hospitalizations
- The case highlights the challenges in managing cardiovascular disease during pregnancy, emphasizing the need for multidisciplinary care and individualized treatment approaches

Case 2 *Learning Points*

- Metoprolol was initiated with SBP ~100
- Especially worrisome: the trend of hospitalizations, diuretic requirements, NYHA class as pregnancy progressed

*We trend BNP and Trop throughout pregnancy

Case 2 *Learning Points*

- Team-based care allowed for smooth transition from outpatient to inpatient management when symptoms dictated
- RHC reserved for patients who continue to have symptoms of heart failure, poor perfusion, organ dysfunction despite diuresis
- RHC can be done safely, with lead covering gravid uterus
  - Radiation risk to the fetus is highest in early pregnancy

Case 2 *Learning Points*

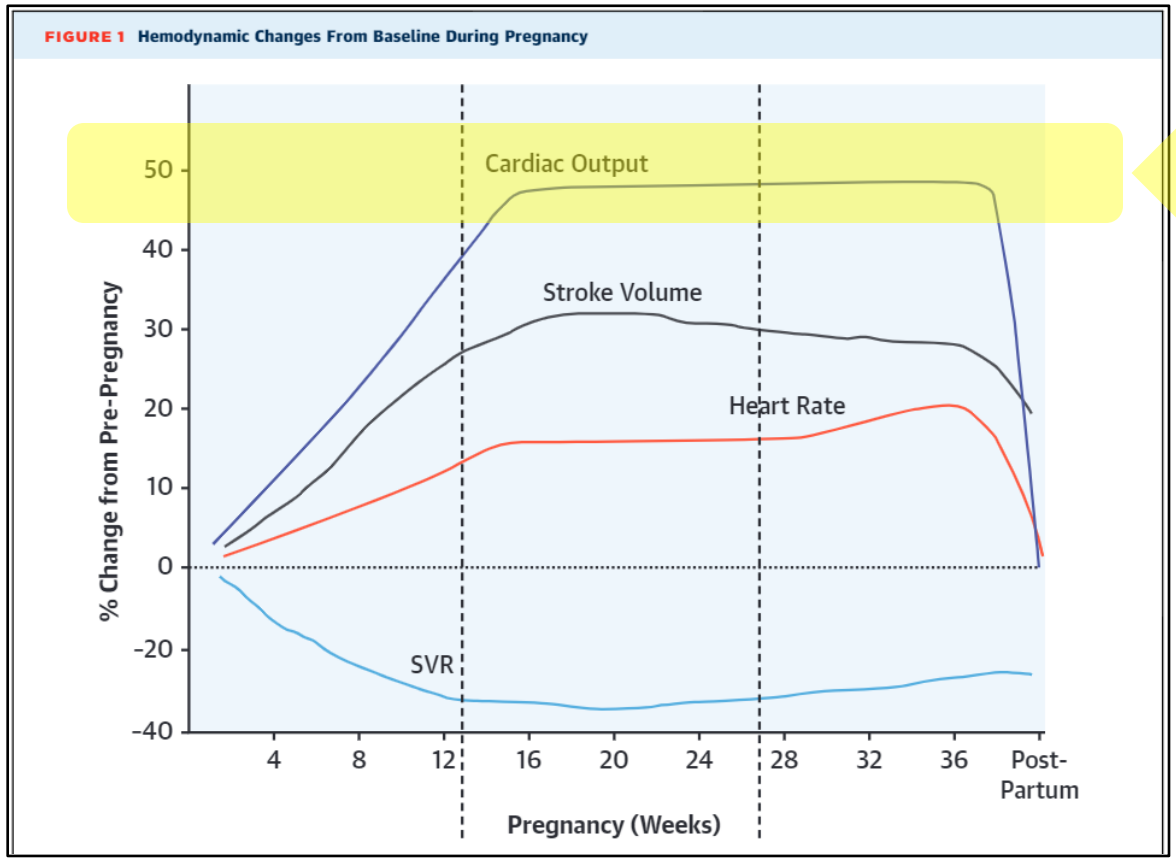
Hemodynamic review:

RA 16, PA 56/22 (39), PW 29
PA sat 50%, Fick CI 1.9, Thermo CI 2.1, SVR 1800

- High filling pressures (more than two-fold)
- Pulmonary pressures are high, so "pulmonary hypertension" is present = WHO group 2, driven by left-sided heart disease

*No indication for pulmonary vasodilators

Case 2 *Learning Points*



Davis et al. Cardio-Obstetrics Part 1/5. JACC Vol. 77, No. 14, 2021. April 13, 2021: 1763-77.

Case 2 *Learning Points*

Hemodynamic review:

RA 16, PA 56/22 (39), PW 29
PA sat 50%, Fick CI 1.9, Thermo CI 2.1, SVR 1800

- Cardiac output/ index should be 50% *more than baseline*, starting 16 weeks of pregnancy
- So cardiac index of ~2 is significantly low, borderline shock

Case 2 *Learning Points*

→ Stopped Bblocker (negative inotropic and chronotropic effects)

→ Switched to pure afterload reduction (hydralazine)

→ Dobutamine was started for hemodynamic stabilization

Case 2 *Learning Points*

- Contraception discussed, patient opted for tubal ligation
- Very few cardiac indications for c-section vs. vaginal delivery
  - Assist second stage in high risk patients
  - Reserve c-section for obstetric indications, oral anticoagulation, severe aortic disease, acute intractable heart failure
    - In our center, patients with acute heart failure/ shock, severe valve disease undergoing c-section may have sheaths placed for urgent ECMO if needed
  - Cohort study (2,921 deliveries of patients with a diagnosis of cardiomyopathy) found high rate of intrapartum c-section, necessitates delivery centers be prepared for urgent, high-risk intrapartum c-section

M-L Meng, JJ Federspiel, ...V Krishnamoorthy, et al. "Severe Maternal Morbidity According to Mode of Delivery Among Pregnant Patients With Cardiomyopathies." JACC Heart Fail. 2023 Dec;11(12):1678-1689.

Case 2 *Learning Points*

- Prepare for autotransfusion following delivery, mediated by release of IVC compression and contracting uterus → massive fluid bolus into maternal circulation
- Bipap, IV loop diuretic on hand to prevent or treat pulmonary edema

Case 2 *Learning Points*

- Consider AC when LVEF <30% (ESC suggests <35%)
  - Lovenox is okay during pregnancy and in breastfeeding
  - Warfarin during pregnancy only for mechanical valves, safe in breastfeeding

  *Avoid DOACs

Brief Case 3

Ischemic heart disease in pregnancy

- 34 year old female with history premature coronary artery disease s/p 1-vessel CABG less than 1 year prior, hyperlipidemia, papillary thyroid cancer now pregnant with first child.
  - ✓ Continued low dose aspirin
  - ✓ Stopped statin (can continue omega 3 fatty acids)

Brief Case 4

Arrhythmia /Channelopathy in pregnancy

- 28 year old female with history of obesity, cardiac arrest during prior delivery leading to diagnosis of Long QT Syndrome and ICD implant, now pregnant with 2nd child.
  - ✓ Continued nadolol once daily throughout pregnancy
  - ✓ Changed to TID propranolol at time of delivery due to interest in breastfeeding

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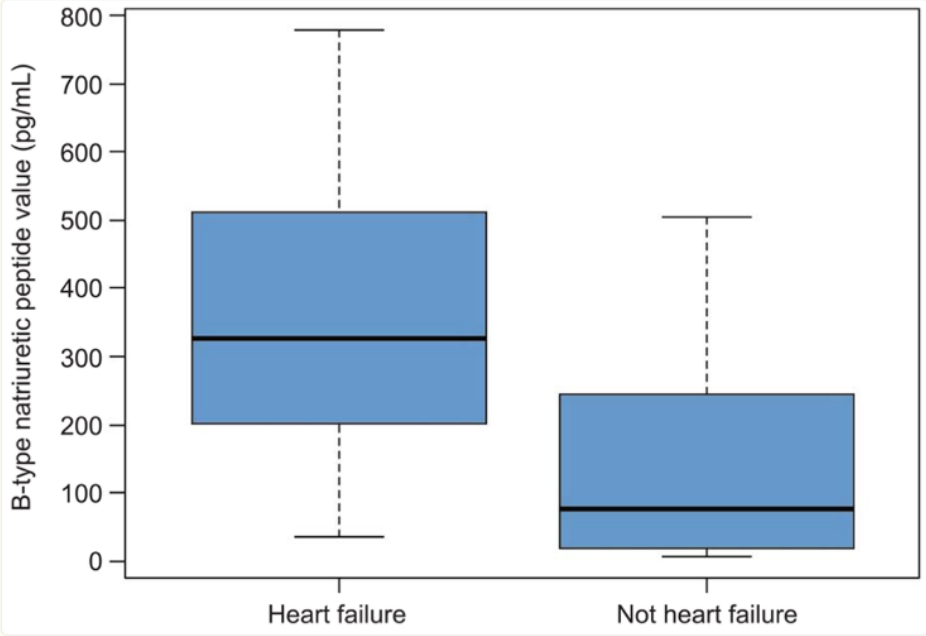
B-Type Natriuretic Peptide

- 22 pregnant and 38 postpartum women were included, average age 32 ± 6.8 years
- Most common clinical features at the time of presentation were chest discomfort (53%), preeclampsia (55%), and dyspnea (83%)

I Malhamé, H Hurlburt, …N Mehta, et al. “Sensitivity and Specificity of B-Type Natriuretic Peptide in Diagnosing Heart Failure in Pregnancy.” Obstet Gynecol. 2019 Sep;134(3):440-449.

B-Type Natriuretic Peptide

- Median BNP was 326 in women with HF, vs. 75 in women without HF
- At a cutoff value of 111 pg/mL, BNP yielded a 95% sensitivity, 62% specificity for the diagnosis of HF



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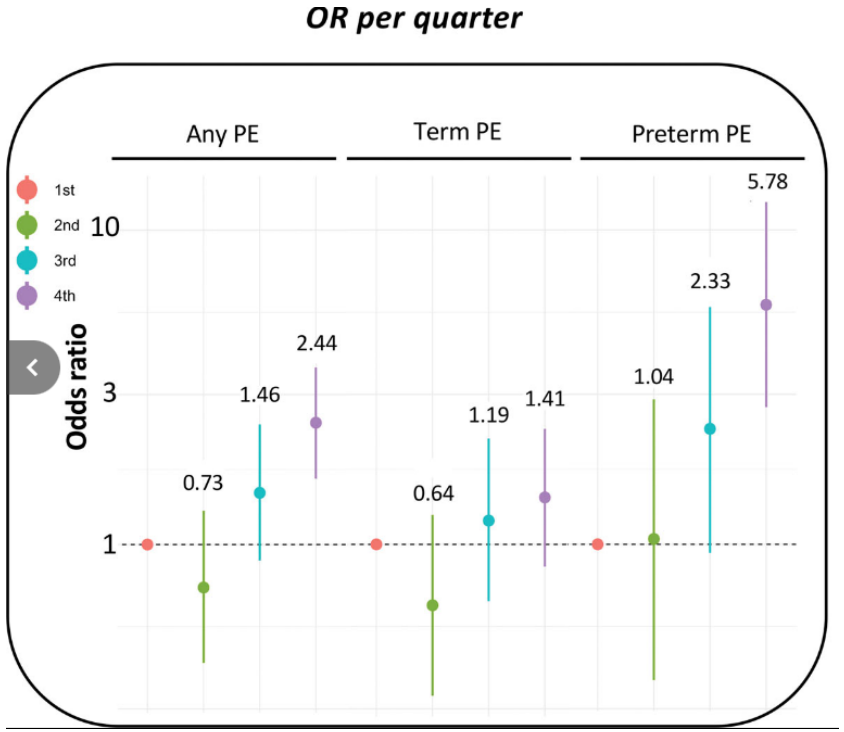
High-Sensitivity Cardiac Troponin I

- This study measured hs-cTnI levels in 3721 blood samples of 2245 pregnant women from 4 international, prospective cohorts

L Bacmeister, A Goßling, …T Zeller, et al. “High-Sensitivity Cardiac Troponin I Enhances Preeclampsia Prediction Beyond Maternal Factors and the sFlt-1/PlGF Ratio.” Circulation. 2024 Jan 9;149(2):95-106.

High-Sensitivity Cardiac Troponin I

- Women with hs-cTnI in the upper quarter had higher odds ratio for pre-eclampsia compared to women with levels in the lower quarter
- Hs-cTnI level ≥1.9 pg/mL may tip the scale toward preventative strategies



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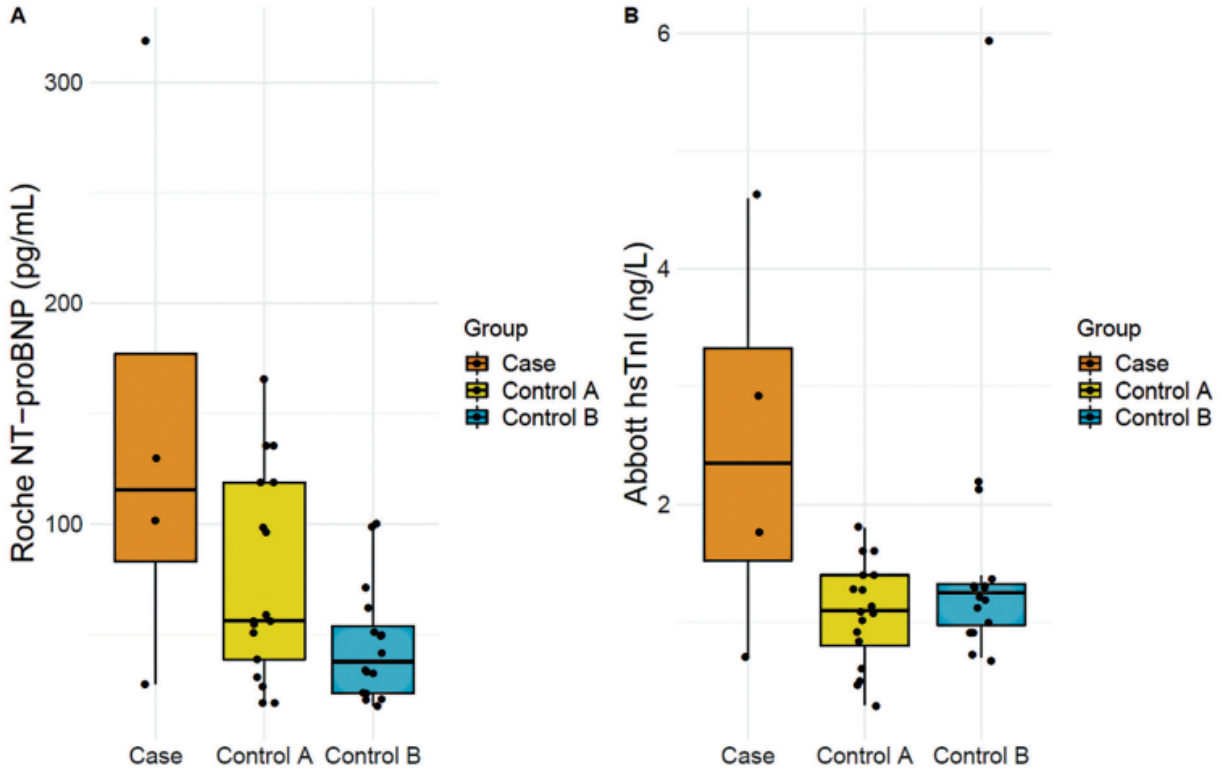
Biomarkers for PPCM

- A retrospective case-control study comparing cases of patients who develop ppcm, matched to unaffected women by age, race, parity, gestational age of sample, then further matched by BP and pregnancy weight gain
- 9930 women who received prenatal care at Mass General between 1998 and 2006, serum sample collected at first prenatal visit

AA Sarma, S Hsu, JL …NS Scott, et al. “First Trimester Cardiac Biomarkers among Women with Peripartum Cardiomyopathy: Are There Early Clues to This Late-Pregnancy Phenomenon?” Am J Perinatol. 2023 Jan;40(2):137-140.

Biomarkers for PPCM



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Biomarkers for PPCM

- NT-proBNP concentrations were higher in the first trimester among those who developed ppcm vs. those who did not
- A higher proportion of women who developed ppcm had detectable hs-cTnI levels, compared to controls
- This suggests that early pregnancy subclinical myocardial dysfunction may be associated with ppcm

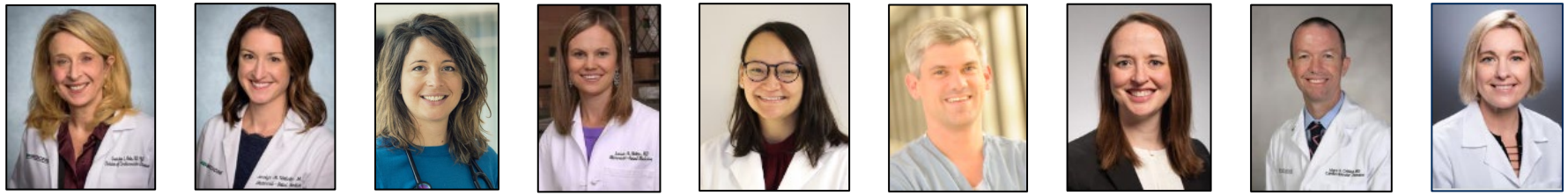
AA Sarma, S Hsu, JL …NS Scott, et al. “First Trimester Cardiac Biomarkers among Women with Peripartum Cardiomyopathy: Are There Early Clues to This Late-Pregnancy Phenomenon?” Am J Perinatol. 2023 Jan;40(2):137-140.

Team-based care

Personalized, specialized care provided by a multidisciplinary, cardio-obstetric team is standard of care for every pregnant woman with pre-existing or newly discovered cardiovascular disease

Team-based care

Our Cardio-Obstetrics team at UAB:



and many more!

Longitudinal Follow-up

- Medication titration, optimization
- ICD if and when indicated
- Cardiac rehab
- Genetic testing
- Future pregnancy counseling
- Referral for advanced therapies if needed

Thank you for your attention.

Discussion