

Optimizing Postpartum Maternal Health to Prevent Chronic Diseases

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Disclosures

- Research:
 - None
- Financial: none applicable to this presentation
 - PRIUM
 - QEssentials Market Research
 - M3 Global Research
 - Medscape
 - Guidepoint

Objectives

Following this presentation, participants will be able to:

1. Recognize the negative impact of gestational diabetes mellitus (GDM) and pregnancy induced hypertension (PIH) on future maternal health.
2. Teach patients and other clinicians the need for aggressive risk modification after GDM and PIH to avoid future chronic disease(s).
3. Initiate the most evidenced based initial management for patients with postpartum hyperglycemia and hypertension.

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Your next clinic patient...

- 42y G2P2002 who presents for her annual evaluation.
- Today her BP is 120/70 and her current weight is 185lbs (BMI of 28.6 kg/m²).
- Her prior obstetric history: gestational diabetes in both pregnancies, gestational hypertension in the second pregnancy only.
- She is asymptomatic.



Based on her obstetric history of gestational diabetes, she is high risk for which diseases?



Hypertension **A**

Heart Failure **B**

Stroke **C**

Hyperlipidemia **D**

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Based on her obstetric history of
hypertension in pregnancy, she is at
risk for which diseases?



Hyperlipidemia

Coronary Artery Disease

Obesity

Arteriod Atherosclerosis

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Half of women with a history of gestational diabetes will develop diabetes mellitus within how many years of the index pregnancy?



Three years

Five years

Seven years

Nine Years

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Which of the following obstetric conditions increases a woman's risk of premature cardiac death?



Gestational diabetes

HELLP syndrome

Preterm Birth

Large birth weight infant

Phospholipid syndrome

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Future Disease Predicted by Pregnancy

- **Hypertension**
 - Prevalence 77.9 million adults
 - Predicted by **GDM and GH**
- **Diabetes Mellitus**
 - Prevalence 26 million adults
 - Predicted by **GDM and GH**
- **Overweight/Obesity**
 - Prevalence 78.6 million adults
 - Predicted by **excess weight gain in pregnancy**
- **Heart Failure**
 - Prevalence 5.8 million adults
- **Stroke**
 - Prevalence 6.3 million adults
- **Chronic Kidney Disease**
 - Prevalence 20 million adults
 - Predicted by **GDM and PIH**
- **Cardiovascular Disease (CHD, CVD, PAD, CHF, VTE)**
 - Prevalence 85.6 million adults
 - **44 million women**
 - Predicted by **GDM and PIH**

Associations of Pregnancy Complications With Calculated Cardiovascular Disease Risk and Cardiovascular Risk Factors in Middle Age

- Prospective cohort of 3,416 women that studied associations of 1) GDM, 2) HDP, 3) preterm delivery, and 4) size for gestational age. A wide range of vital signs and cardiovascular risk factors were measured for 18 years after pregnancy and 10-year CVD risk (Framingham score) was calculated.
- Compared to the women without preeclampsia and/or GDM, the future risk of CVD for women with prior preeclampsia had an OR of 1.31 and women with prior gestational diabetes had an OR of 1.26.
- Hypertensive disorders of pregnancy and pregnancy diabetes mellitus are independently associated with an increased calculated 10-year Framingham CVD risk and preeclampsia is the best predictor of future CVD because it is associated with a wider range of cardiovascular risk factors than HDP and GDM alone.

Circulation, Feb 2012

Cardiovascular risk factors in women who had hypertensive disorders late in pregnancy

- Multicenter cohort study of 306 women with a history of HTP and women with a history of normotensive pregnancies at term (N = 99) in The Netherlands from 2008-2010 to **determine cardiovascular risks 2.5 years after pregnancy.**
- **Hypertension and metabolic syndrome were more prevalent** in HTP women compared with NTP women
- Women with HTP had higher **SBP and DBP, higher BMP, and higher WC.** They also had **significantly higher** glucose, A1c, TC, TG, and **hs-CRP** levels with **significantly lower** HDL

American Journal of Obstetrics and
Gynecology, June 2012

Elevated blood pressure in pregnancy and subsequent chronic disease risk.

- The Northern Finland Birth Cohort of 1966 included 12,055 women, and records from 10,314 women were reviewed.
- PIH is associated with **increased risk of ischemic heart disease, MI, CHF, Ischemic stroke, CKD & DM.**
- Women with chronic hypertension *and* superimposed preeclampsia or eclampsia had **high risk** for future diseases.
- **Clinical monitoring, risk factor evaluation, and early intervention could benefit women with hypertension in pregnancy.**

Circulation, Feb 2013

Stroke Prevention in Women

- Preeclampsia occurs in approximately 5% of pregnancies. A history of preeclampsia is associated with a 2-fold risk for stroke.
- After pregnancy:
 - All women with a history of preeclampsia would probably benefit from lifestyle change and early assessment of cardiovascular risk and interventions.

Ann Intern Med. June 2014

Gestational diabetes mellitus and later cardiovascular disease

- Population-based case–control study of 2,639 women from the National Swedish register data from 1991-2008 who had an 1) ischemic heart disease, 2) ischemic stroke, 3) atherosclerosis or 4) peripheral vascular disease.
- Conditional logistic regression examined association of GDM with CVD by BMI, smoking and HTN before and after adjustment for conventional risk factors, confounders post-pregnancy diabetes.
- The adjusted odds ratios for association of CVD with GDM is 1.51, smoking is 2.23, obesity is 1.98, and HTN is 5.10.
- In stratified analysis the association of CVD with GDM was only seen among women with BMI ≥ 25 and < 30 , with an odds ratio of 2.39 and adjustment for post-pregnancy diabetes attenuated the OR to 1.99

British Journal of Obstetrics & Gynecology, Nov 2014

Gestational diabetes mellitus is a significant risk factor for long-term maternal renal disease

- Population-based non-interventional study at an academic medical center including **97,968 women with prior singleton pregnancies** with and without prior GDM during a **25-year period** to investigate whether GDM poses a risk for long-term maternal renal morbidity.
- Of the study population, **9542 (9.7%) had at least 1 previous pregnancy with GDM**. Women with GDM had significantly higher rates of total renal morbidity.
- In a Cox proportional hazards model, adjusted for confounders, **GDM was independently associated with future renal morbidity**. Additionally, the risk is more substantial for patients with **recurrent episodes** of GDM.

J Clin Endocrinol Metab, April 2015

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Cardiovascular disease risk is only elevated in hypertensive, formerly preeclamptic women

- Observational study in a tertiary referral hospital in The Netherlands that analyzed the predicted 10- and 30-year risk scores for CVD in patients who experienced preeclampsia (PE) 5–10 years previously vs healthy women with similar obstetric histories.
- There were 115 preeclampsia patients in two groups, hypertensive ($n = 21$) and normotensive ($n = 94$), and next sub-categorized based on the onset of preeclampsia: **early-onset ($n = 39$) versus late-onset PE ($n = 76$).**
- All participants underwent cardiovascular risk screening **5–10 years after index pregnancy including BMI, BP, fasting glucose, insulin and lipid levels.**

British Journal of Obstetrics and
Gynecology, Aug 2014

Cardiovascular disease risk is only elevated in hypertensive, formerly preeclamptic women

- **Hypertensive** versus normotensive women with **history** of preeclampsia had **twice the CVD risk**.
- Patients with history of **early-onset preeclampsia** clustered more often in the **hypertensive** group and showed **significantly higher** 10- and 30-year CVD risk estimates.
- Women who **are normotensive in the first 10 years** after their preeclamptic pregnancy have a **comparable future cardiovascular risk** to healthy controls.
- **"We stress the importance of ongoing surveillance which at present we do not think is practiced consistently"**

British Journal of Obstetrics and
Gynecology, Aug 2014

The effect of lifestyle intervention and metformin on preventing or delaying diabetes among women with & without gestational diabetes

- RCT conducted at 27 clinical centers with observational follow-up that evaluated lifestyle versus metformin versus standard care **over 10 years in women with and without prior GDM** (N = 350, 1416 respectively) who had an entry BMI >24 and also had IGT.
- Women with a history of GDM assigned to **placebo** had a **48% higher risk of developing diabetes**.
- Conversely, women assigned to **lifestyle changes** and **metformin** had progression to diabetes **reduced 35% and 40%**, respectively.

Journal of Clinical Endocrinology & Metabolism, Apr 2015

Metformin versus Placebo in Obese Pregnant Women without Diabetes Mellitus

- Double-blind intention-to-treat RCT that assigned pregnant women at **12 to 18 weeks gestation**, **without diabetes** and **with a BMI >35** at study entrance were treated with 3000mg daily metformin, or placebo (225 women in each group).
- The primary outcome was a reduction in the median neonatal birth-weight with secondary outcomes of **maternal gestational weight gain and the incidence of GDM and preeclampsia**, as well as the incidence of adverse neonatal outcomes.
- **Median maternal gestational weight gain was lower in the metformin group** (4.6 kg vs. 6.3 kg; $P<0.001$), **as was the incidence of preeclampsia** (3.0% vs. 11.3%; $P=0.001$).

NEJM, Feb 2016

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Postpartum Hypertension

Medications

- Oral **nifedipine** improves renal blood flow with resultant diuresis. IV hydralazine pairs well with this for inpatient acute treatment.
- An **ACE Inhibitor** should be started for all diabetics or postpartum cardiomyopathy patients.
- **Diuretics** may be needed in women with volume overload. **Spironolactone** is a good choice for African American women.

REMINDERS!!

1. Agents with high protein binding and low lipid solubility are less likely to be transferred in breast milk.
2. Breastfeeding is not a reliable method of contraception

Discharge Planning

- Goal blood pressure for a safe discharge is **<150/90** in healthy women, **<140/90** in women with chronic hypertension and **<140/80** in women with and/or diabetes mellitus
- Instruct women to measure blood pressure at least once daily and report any symptoms until her next visit in 1 week.
- **SAFETY**: Teach women prior to discharge the appropriate ways to measure blood pressure to avoid 1) falsely elevated measurements and 2) continuation of unnecessary medications.

Outpatient follow-up

- Check renal function within one week for patients on diuretics and ACE inhibitors.
- Antihypertensive medications are discontinued if the BP remains below the hypertensive levels for at least 48 hours.
- All women with any form of hypertension affecting pregnancy deserve a follow-up appointment to 1) confirm blood pressure normalization, 2) stop unnecessary medications, and 3) evaluate for etiologies of secondary hypertension in women <40 years.

Future Screening

- Women with history of hypertensive disorders in pregnancy, including preeclampsia, **need annual monitoring of risk factors.**
- Ideal timing varies but is **not later than 1 year postpartum.**
- Screening should include evaluation for risk factors including: **BP, BMI, smoking, alcohol, sleep quality and activity level.** Annual labs should include: **glucose, creatinine, urinalysis, and lipids.**

Clinical Science, Jan 2016

Postpartum Hyperglycemia

Normal Postpartum Glucose

- If **fasting glucose** postpartum is **<100** (normal):
 - TEACH: the woman of her **elevated lifetime risk** for diabetes mellitus, heart disease and stroke
 - TEST in 6-12 weeks with postpartum screening
 - TREAT with increased physical activity and healthy nutrition.

Future Screening:

- Test women with history of GDM every 1-3 years if OGTT at 6-12w is **normal**
 - Frequency of screening is based on risk factors: family history, pre-pregnancy BMI, need for diabetic medications during pregnancy, etc
- Ongoing screening may include A1c, FPG, OGTT using non-pregnancy values
- 1) Metformin and 2) intensive lifestyle changes prevent or delay progression to diabetes mellitus

American Diabetes Association, Jan 2016

Prediabetes

- If postpartum **fasting glucose** is **100-125**, the patient has **prediabetes**
 - TEACH the woman of her **elevated lifetime risk** for diabetes mellitus, heart disease and stroke
 - TREAT with intensive lifestyle changes and if A1c is 5.7%-6.4%, add metformin XL 750mg
 - SCREEN annually thereafter for glucose abnormalities

Diabetes Mellitus

- If **fasting glucose** postpartum is **>126**, repeat the test in 24 hours to confirm the diagnosis of **diabetes mellitus**
 - TEACH the women of her **elevated lifetime risk** for heart disease, kidney disease and stroke
 - TREAT with intensive lifestyle changes including a diabetic diet, metformin XL 750mg twice daily with meals +/- other diabetic medications if A1c >8%
 - SCREEN for nephropathy (microalbumin/creatinine ratio >30) and if present, start an ACEI (lisinopril 2.5mg qd if not breastfeeding)

Key Points

- GDM and PIH have a significant negative impact on future maternal health and are opportunities for intensified preventive medicine.
- All women with history of gestational diabetes, gestational hypertension and preeclampsia need annual evaluation within the first 6-12 months of delivery to optimize health.
- Women with a history of GDM should be treated metformin and/or intensive lifestyle changes to prevent development of diabetes

Your next clinic patient...

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- Today her BP is 120/70 and her current weight is 185lbs (BMI of 28.6 kg/m²).
- Her prior obstetric history: gestational diabetes in both pregnancies, gestational hypertension in the second pregnancy only.
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Question 1

Based on her history of **gestational diabetes**, this patient is at increased risk of which of the following?

- Hyperlipidemia
- Obesity
- Hypertension
- Cardiovascular Disease

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- **Cardiovascular Disease**

Gestational diabetes mellitus and later cardiovascular disease

Rationale: the presence of gestational diabetes in women without other risk factors for cardiovascular disease, such as obesity, hypertension or smoking, is associated with future cardiovascular in women with a BMI between 25.0-29.9. This is statistically significant and may be the only identifiable risk factors in women under age 45 years who otherwise appear healthy and are asymptomatic. Care should be taken to collect a thorough obstetric history at each prevention visit and to screen these women for other abnormalities, such as low HDL (under 50 in women).

Citation: Fadl H, Magnuson A, Östlund I, Montgomery S, Hanson U, Schwarcz E. Gestational diabetes mellitus and later cardiovascular disease: a Swedish population based case-control study. *British Journal of Obstetrics & Gynecology*, Nov 2014

Question 2

Based on her history of **gestational hypertension**, this patient is at increased risk of which of the following?

- Hyperlipidemia
- Obesity
- Prediabetes
- Stroke

Question 2

Based on her history of **gestational hypertension**, this patient is at increased risk of which of the following?

- Hyperlipidemia
- Obesity
- Prediabetes
- **Stroke**

Elevated blood pressure in pregnancy and subsequent chronic disease risk.

Rationale: gestational hypertension is independently associated with future stroke with a hazard ratio of 1.78 (confidence interval: 1.43-2.21). Hypertension during pregnancy is associated with arterial hypertension. Clinical monitoring, risk factor evaluation, and early intervention could benefit women with hypertension in pregnancy.

Citation: Männistö T1, Mendola P, Vääräsmäki M, Järvelin MR, Hartikainen AL, Pouta A, Suvanto E. Elevated blood pressure in pregnancy and subsequent chronic disease risk. *Circulation*, Feb 2013.

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“Pregnancy ...

an opportunity to identify women at increased risk...

*allowing lifestyle changes and, if required, other
interventions aimed at reducing that risk...*

earlier in the life course”

Circulation, Feb 2012