

UNDER PRESSURE

Preeclampsia at any stage of pregnancy is always cause for concern. When it sets in early, however, it can strike at the heart of health for women

Nausea. Fatigue. Bizarre food cravings. These are the symptoms most people associate with pregnancy.

Ranging from mild to severe, these symptoms are generally more of a nuisance than a true harm. A more serious complication of pregnancy is preeclampsia, which occurs in 5% to 7% of all pregnancies, and is characterized by high blood pressure and excess protein in the urine.

Because our bodies rely on the healthy circulation of blood throughout to supply organs and tissues with vital nutrients and oxygen, arteries damaged by high blood pressure lead to a host of serious health problems. Thus, preeclampsia poses threats to both mother and baby. In the former: brain injury, impaired liver and kidney function, blood clots, fluid in the

lungs and seizure; in the latter, premature birth, poor growth and even death.

"Preeclampsia is a placental disease, and it's the leading cause of maternal and fetal morbidity and mortality in the developed world," says Dr. Michelle Hladunewich, an associate scientist in the Women & Babies Research Program at Sunnybrook Research Institute. "One of the biggest risk factors is increasing maternal age, and as we keep waiting to have our babies, preeclampsia is becoming more common."

She would know. Hladunewich leads the divisions of obstetrical medicine and nephrology within the department of medicine at Sunnybrook Health Sciences Centre, and treats women in the Greater Toronto Area with any form of kidney disease in pregnancy, including preeclampsia.

Preeclampsia was once thought to be a self-limiting condition that resolved itself after delivery of the placenta, but research, notably, a population-based cohort study published in the *British Medical Journal* in 2001, has shown that women with preeclampsia are at increased risk of death from cardiovascular causes. "When you look at the epidemiological studies, a few patterns emerge: the earlier the onset of preeclampsia, the more severe your preeclampsia, whether your baby lived or died—all indicate that the more sick your placenta was, the worse was your cardiovascular risk later in life," says Hladunewich.



DR. MICHELLE HLADUNEWICH AND ELISA MARTINEZ-REYES

She has taken this important insight even further in a paper published in *Circulation* in October 2010. In it, she and her colleagues showed that among women studied who had placental disease, only those who had early-onset preeclampsia or intrauterine growth restriction without preeclampsia (IUGR, a condition marked by poor fetal growth), showed impaired vascular function, pointing to higher future risk of vascular disease.

In the study, women at one-year postpartum were divided into four groups: those who had early-onset preeclampsia (before 34 weeks gestation), late-onset preeclampsia (after 34 weeks gestation), IUGR without preeclampsia and prior normal pregnancy. Hladunewich found that the women who had early-onset preeclampsia, as well as those with IUGR without preeclampsia, had stiffer arteries than did those in the other two groups.

She also found that these women had reduced flow-mediated dilatation, a test used to detect early vascular disease. The more a blood vessel dilates in response to hyperemic stress—as in the squeeze of a blood pressure cuff—the healthier it is; a vessel that dilates less indicates dysfunction in the endothelium (the inner lining of the blood vessel). Again, there was less dilatation of the main blood vessel of the upper arm only in the women who had early-onset preeclampsia and IUGR without preeclampsia. Moreover,

the degree of dilatation in the arteries of the women who had late-onset preeclampsia was similar to that of the healthy control subjects.

Stiff arteries and decreased flow-mediated dilatation are standard measures of vascular dysfunction (damaged blood vessels), which is a precursor to cardiovascular disease. “Our hypothesis that there would be differences depending on the disease was borne out,” says Hladunewich. Other researchers have looked at the risks of hypertension during pregnancy; this study is unique in that it differentiated between early- and late-onset preeclampsia. “We were very careful about which women went into which group, which is why we got cleaner, more interesting results than did previous studies,” she says.

While she expected to see differences in vascular function among women with early- and late-onset preeclampsia, Hladunewich says that the extent of endothelial dysfunction in the women who had IUGR and normal blood pressure came as a surprise. She reviewed the ultrasound images of the women’s placentas from their pregnancies and found that those who had poor blood flow to the placenta were the same women who exhibited endothelial dysfunction. “It’s the placenta that can give us predictive value of who’s at risk of future vascular disease,” she says.

For Hladunewich, the implication of this research for clinical practice is clear:

“It’s time to pay attention to this complication of pregnancy because we can change women’s lives,” she says. She wants family doctors and members of the general public, especially women, to know that preeclampsia is as much of a risk factor for heart disease as are age, family history and cholesterol profile.

Educating stakeholders on the relevance of pregnancy history to future cardiovascular disease is a challenge. Primary care doctors contending with massive patient loads find it near impossible to stay abreast of the latest research in all the fields applicable to their practice. Moreover, with the shortage of family doctors in Ontario, many of the patients Hladunewich sees only begin receiving health care during their pregnancies. For these reasons she is passionate about teaching and empowering her patients who have preeclampsia. “[To] every single preeclamptic woman I see in this clinic, I say, ‘You need to be an advocate of your health.’ These women got an early warning sign, and they need to capitalize on that. If nothing else, we could teach young women early on to eat well, exercise and watch their salt intake—to live healthy-heart lifestyles.”

— Alisa Kim

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