Immune system can detect disease during pregnancy

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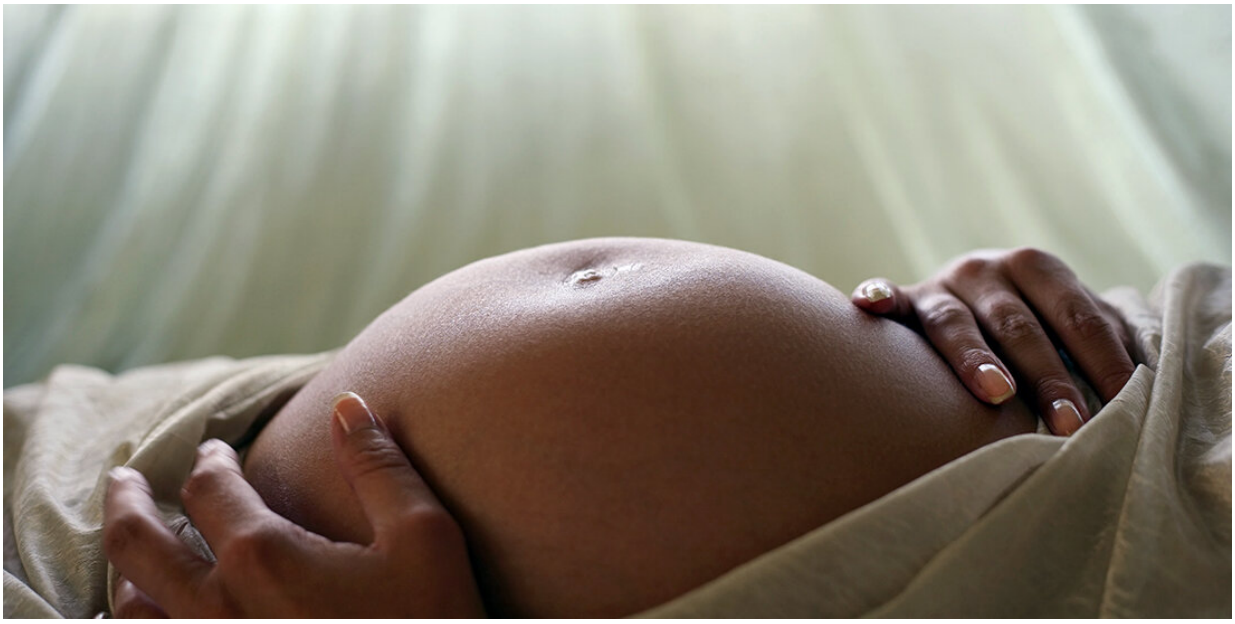

Researchers now have an overview of how the immune system behaves in normal pregnancies that they can use as a reference for what is normal. The next step is to gain an overview of changes that are brought on by pregnancy complications. Credit: Colourbox

Pregnancy is a challenge for the mother's immune system from the outset. Half of the genes in the fetus are foreign to her body.

The immune system has to strike a balance between tolerating the fetus

and protecting the mother and fetus from infections. Throughout the pregnancy, an immunological balance takes place between mother and child.

At NTNU's Centre for Molecular Inflammation Research (CEMIR), a research group is engaged in studying inflammation in pregnancy. The group has made findings that shed light on how the immune system behaves during pregnancy.

707 pregnant subjects

Anders Hagen Jarmund, a research program student, and his colleagues at CEMIR are the first researchers to survey the development of women's immune responses throughout pregnancy.

The study followed 707 women with normal pregnancies, who gave birth to healthy full-term and post-term babies.

"Our immune system is regulated by cell signaling molecules called cytokines. The signaling molecules can trigger or stop immune responses. We profiled a number of different cytokines in the blood using a simple blood sample from the mother. Linking the measurements of lots of cytokines at several points in the pregnancy gave us an imprint of the mother's immune response," says Jarmund.

"Because we have so many healthy pregnant women in the study, we were able to find the 'standard' for how the immune system behaves during normal pregnancies," he says.

"Standard" pregnancy

Blood samples from the mother provide detailed information about

inflammatory conditions in the body, the strain on the fetus and early signs of immunological disorder.

The researchers found that immune activity in normal pregnancies follows a certain pattern, with elevated immune activation in the first three months, then a calmer phase the next three and higher activity in the last three months, especially when childbirth is imminent

Finding abnormalities

Jarmund believes that studying the immune system's behavior in normal pregnancies can be very useful.

"Our study can serve as a reference for what's normal at different stages throughout pregnancy. By comparing analyses of blood samples from the pregnant woman with our survey, we can detect abnormalities very early," Jarmund said.

"Early detection can help the doctor assess whether the woman has an increased risk of developing a disease and needs extra close follow-up."

Risk factors

Jarmund discovered several conditions in the mother or fetus that created abnormalities in the immune response.

"The immune changes detected with cytokine profiling are so sensitive that they capture the effects of obesity and smoking in the mother. The immune system is also affected if the fetus is stunted, and may even indicate whether it's a boy or a girl," says Jarmund.

Another finding was that women who had given birth previously clearly

had higher immune activation in the beginning of their pregnancy, but lower than first-time mothers as labor approached. Women who went over term had particularly strong immune activation, which might indicate stress.

Method used for PCOS

Live Marie T. Stokkeland is a Ph.D. candidate at the same center as Jarmund, as well as at the Women's Health and PCOS group led by Professor Eszter Vanky. Stokkeland is studying a group of women with PCOS (polycystic ovary syndrome).

PCOS is a hormonal disorder characterized by increased levels of male hormones and blisters on the ovaries. About 17 percent of women of childbearing age are affected.

Women with PCOS often experience irregular menstruation, overweight and increased hair growth on the face and body, and they often struggle to conceive.

The risks for women with PCOS during pregnancy include preeclampsia, gestational diabetes and premature birth.

Increased activity in the immune system

Stokkeland analyzed blood samples from 358 women with PCOS and a sample group of healthy women.

She found that women with the disease have higher immune activation throughout pregnancy than healthy women, and their immune response developed differently during the three phases of pregnancy.

Women with PCOS who smoked or were overweight showed even stronger immune activation.

"We believe that the overactive cytokines in pregnant women with PCOS are an unfavorable response that indicates stress, and that may be a contributing factor to an increased risk of complications. We hope that further research will tell us more about the causes of adverse responses and what can be done to prevent them," says Stokkeland.

Finding high-risk pregnancies

Professor Ann-Charlotte Iversen, who leads the group that is studying inflammation in pregnancy, believes the two studies offer exciting perspectives.

"A cytokine profile is a very sensitive measurement of the immune system, and now we have a better understanding of the immune system's normal development in pregnancy and how it's affected," says Iversen.

"Once we've mapped the changes that characterize various pregnancy complications, it will show us which abnormalities we should look for in order to detect disease development as early as possible. Having this sensitive a method will enable us to point out high-risk pregnancies so we can follow up the mother and fetus more closely. That's our goal," says Iversen.

The research group at the Department of Clinical and Molecular Medicine does not yet know whether each individual disease generates a unique "fingerprint" in the immune response. So far, the analyzes have revealed an abnormal cytokine profile for PCOS and gestational hypertension (high blood pressure) in early pregnancy.

The research was published in *Frontiers in Immunology* and *The Journal*

of Clinical Endocrinology & Metabolism.

More information: Anders Hagen Jarmund et al, Cytokine Patterns in Maternal Serum From First Trimester to Term and Beyond, *Frontiers in Immunology* (2021). DOI: 10.3389/fimmu.2021.752660

Live Marie T Stokkeland et al, Changes in Serum Cytokines Throughout Pregnancy in Women With Polycystic Ovary Syndrome, *The Journal of Clinical Endocrinology & Metabolism* (2021). DOI: 10.1210/clinem/dgab684

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