Preterm birth linked to chemicals found in the vagina

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Chemicals that accumulate in the vagina, potentially originating from personal care products, may contribute to spontaneous preterm birth, according to a new study by researchers at Columbia University Vagelos

College of Physicians and Surgeons.

The study of 232 pregnant women found that a handful of non-biological chemicals previously found in cosmetics and hygiene products are strongly associated with preterm birth.

"Our findings suggest that we need to look more closely at whether common environmental exposures are in fact causing preterm births and, if so, where these exposures are coming from," says study co-leader Tal Korem, Ph.D., assistant professor in the Program for Mathematical Genomics and the Departments of Systems Biology and Obstetrics and Gynecology at Columbia. "The good news is that if these chemicals are to blame, it may be possible to limit these potentially harmful exposures."

The study was published January 12 in *Nature Microbiology*.

Preterm birth, childbirth before 37 weeks of pregnancy, is the number one cause of neonatal death and can lead to a variety of lifelong health issues. Two-thirds of preterm births occur spontaneously, but despite extensive research, there are no methods for predicting or preventing spontaneous preterm birth.

Several studies have suggested that imbalances in the vaginal microbiome play a role in preterm birth and other problems during pregnancy. However, researchers have not been able to reproducibly link specific populations of microorganisms with adverse pregnancy outcomes.

The research team, co-led by Korem and Maayan Levy, Ph.D., of the University of Pennsylvania, decided to take a more expansive view of the vaginal microenvironment by looking at its metabolome. The metabolome is the complete set of small molecules found in a particular

biological niche, including metabolites produced by local cells and microorganisms and molecules that come from external sources. "The metabolome can be seen as a functional readout of the ecosystem as a whole," Korem says. "Microbiome profiling can tell us who the microbes are; metabolomics gets us close to understanding what the microbes are doing."

In the current study, the researchers measured over 700 different metabolites in the second-trimester metabolome of 232 pregnant women, including 80 pregnancies that ended prematurely.

The study found multiple metabolites that were significantly higher in women who had delivered early than in those who delivered at full term.

"Several of these metabolites are chemicals that are not produced by humans or microbes—what we call xenobiotics," says Korem. "These include diethanolamine, ethyl-beta glucoside, tartrate, and ethylenediaminetetraacetic acid. While we did not identify the source of these xenobiotics in our participants, all could be found in cosmetics and hygiene products."

Algorithm predicts preterm birth

Using machine learning models, the team also developed an algorithm based on metabolite levels that can predict preterm birth with good accuracy, potentially paving the way for early diagnostics.

Though the predictions were more accurate than models based on microbiome data and maternal characteristics (such as age, BMI, race, preterm birth history, and prior births), the new model still needs improvement and further validation before it could be used in the clinic.

Despite the current limitations, Korem says, "our results demonstrate

that vaginal metabolites have the potential to predict, months in advance, which women are likely to deliver early."

More information: William F. Kindschuh et al, Preterm birth is associated with xenobiotics and predicted by the vaginal metabolome, *Nature Microbiology* (2023). DOI: 10.1038/s41564-022-01293-8

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