

# NTU Singapore scientists and KKH clinicians develop urine test that identifies pregnancy outcome after threatened miscarriage

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Researchers at **Nanyang Technological University, Singapore (NTU Singapore)** and clinicians at **KK Women's and Children's Hospital (KKH)** have developed a urine test that within 30 minutes, can gauge pregnancy outcomes for women presenting with signs of threatened miscarriage.

Threatened miscarriage – characterised by abdominal pain with vaginal bleeding – is one of the most common gynaecological emergencies worldwide.

According to a separate study by Duke-NUS, NTU and KKH [1], one in five pregnancies in Singapore shows signs of threatened miscarriage within the first trimester. Among pregnant women with such symptoms, one in four of them ends up losing their baby within two weeks.

Clinicians do not currently have a way of predicting their risk of miscarriage that is non-invasive. The current lab-based method assesses a pregnant woman's miscarriage risk through a blood test (serum progesterone test) that measures progesterone levels and can take a few hours.

The new test developed by NTU scientists in collaboration with doctors from KKH uses an innovative surface-enhanced Raman scattering (SERS) chip that requires a droplet of urine to screen for urine molecules associated with miscarriage risk. It does this through the chemical 4-mercaptophenylboronic acid (MPBA) which is coated on the chip. MPBA probes and selectively captures the miscarriage-related molecules pregnane and tetrahydrocortisone (THC) from the urine.

In a case-control study of 40 pregnant women who attended the Urgent O&G Centre at KKH with symptoms of threatened miscarriage, the test retrospectively identified accurately the pregnancy outcomes of all participants.

Led by **Associate Professor Ling Xing Yi** and **Associate Professor Tan Nguan Soon** from NTU, in collaboration with KKH's **Dr Ku Chee Wai**, the study findings were published in the peer-reviewed journal ACS Nano in February 2020.

The researchers believe their initial success points the way towards a non-invasive, fast, and accurate approach for triaging pregnant women with a threatened miscarriage, identifying those who are at higher risk of a spontaneous miscarriage.

**Assoc Prof Ling**, of NTU's School of Physical and Mathematical Sciences, said, "Usually molecules associated with miscarriage risk are simply too dilute within the body's fluids and challenging to detect at low concentrations. To solve this problem, our group developed an innovative SERS 'confine and capture' approach and used a chemical 'targeting agent' to isolate miscarriage-related biomarkers from urine, resulting in speedy detection of miscarriage risk."

**Assoc Prof Tan**, a metabolic disorder expert at NTU's Lee Kong Chian School of Medicine, explained that the unparalleled sensitivity offered by the SERS test and the small sample volume required make it attractive for clinical use.

"This is even more so for cases where large amounts of sample are hard to obtain, such as tear sampling for eye disorders or breath vapour for lung diseases. Our diagnostic platform could revolutionise metabolite detection for medical conditions that

are normally challenging to detect and bring testing for them out of the lab and into the clinic," said Assoc Prof Tan,

**Fast detection removes undue anxiety for patients presenting with threatened miscarriage in the first trimester**

When a woman presents with threatened miscarriage, a reliable and non-invasive diagnostic test would be invaluable for miscarriage risk management say the researchers. However, there is currently no point-of-care test with a quick turnaround time.

**Dr Ku Chee Wai**, Division of Obstetrics and Gynaecology, KKH, said, "This non-invasive toolkit will enable clinicians to predict risk of a spontaneous miscarriage in women who presents with a threatened miscarriage. Early detection will also allow these pregnant women to receive counselling, medical interventions, or be under close medical management for adverse pregnancy outcomes throughout the rest of their pregnancy. It can also allay the fears and worries of pregnant women who are at low risk of miscarriage and improve their pregnancy experience".

**Associate Professor Tan Hak Koon**, Chairman, Division of Obstetrics and Gynaecology, KKH, said, "As the largest academic medical centre specialising in women's and children's health in Singapore, KKH has been leading many progesterone and miscarriage-related studies for over a decade. Our research into SERS steered us towards this collaboration with NTU, advancing both KKH and NTU towards the goal of improving the health outcomes of pregnant women and their babies everywhere in the world."

The NTU team has patented the innovation and is now looking to evaluate the performance of the toolkit in hospital settings, with the aim of commercialising the product in future.

The researchers are also working on adapting the toolkit for use in other types of health conditions.