

Non-invasive biomarkers to diagnose infant urinary tract obstruction

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One in every 500 babies is born with a condition called ureteropelvic junction obstruction (UPJO), an obstruction of the ureter that prevents urine from flowing from one or both of the kidneys into the bladder. Usually diagnosed prenatally, UPJO can cause urinary tract infections and poor growth for infants; it can also result in chronic kidney disease and an increased risk for cardiovascular disease in later life.

A group of researchers at UConn Health, the University of Connecticut, Children's Hospital and Medical Center of Omaha, and Kravis Children's Hospital at the Mount Sinai Health System have developed a panel of five biomarker proteins for the diagnosis and monitoring of UPJO in infants and toddlers. They describe this non-invasive, cost-effective method of detecting and monitoring UPJO in a recent issue of the *Journal of Pediatric Urology*, and are hopeful this technology could be a breakthrough for those suffering from UPJO.

"Normally, the kidneys filter blood and remove waste in the form of urine that drains from the kidneys through the ureters to the bladder,"

explains Linda Shapiro, co-author of the study and UConn Health professor of cell biology and director of the Center for Vascular Biology. "For patients with UPJO, the infant is born with a block in the ureter that causes a backup of urine in the kidney resulting in distension, stretching, and damage to the kidney."

UPJO is a model system for other congenital anomalies of the urinary tract, the most common cause of renal failure in children.

Most of the time, [kidney](#) enlargement, or hydronephrosis, due to UPJO is detectable in the womb by ultrasound. Sometimes UPJO will resolve itself naturally, while other children require surgery. Urologists engage in a "watchful waiting" approach to determine if a child must undergo surgery. Unfortunately, during this period children may suffer irreversible damage to their developing kidneys. This biomarker panel could potentially be used to determine the severity of the damage resulting from obstruction and whether surgery is necessary.

Many molecules have been identified as biomarkers, but there is yet to be a "gold standard" for this condition, emphasizing an immediate need to develop noninvasive biomarkers to detect the severity of damage wrought by UPJO.

This study assessed [urine samples](#) from 22 males under two years old who were on their way to surgery with severe obstruction and samples from a group of 22 control patients who did not have UPJO. The researchers chose males for this pilot study as males are significantly more likely to have UPJO than females.

The researchers began by identifying 171 proteins detectable in the patients with UPJO but undetected in a majority of the controls. Of those 171, only 50 were present in more than half of the UPJO samples. These 50 were ranked using a diagnostic odds analysis to determine the top 10

that may be the most useful biomarkers for this condition. Five of those 10 proteins were found to be present at significantly higher concentrations in patients with UPJO than the control samples, thus creating the panel.

"If it works out well, we'd love to see it transition to the clinic," says Shapiro. "This work can potentially help patients, rather than being just another line in a textbook."

This invention, for which the researchers have filed a patent application, could potentially replace current diagnostic approaches which include expensive, invasive techniques.

This process is non-invasive and painless for the infants. Rather than the current standard of care that entails injecting babies with radiotracers or putting them through other painful procedures, this panel allows practitioners to simply test urine released directly from the bladder.

By using a panel of five biomarkers, the researchers took a probability approach. If a sample had only one or two of the markers, this did not necessarily indicate UPJO damage, but if the sample contained four or five of the markers, the probability they had UPJO was much higher.

Other current methods use a cutoff approach looking at if a patient has a certain concentration of a biomarker. But this approach is inconsistent across patient groups and it can be difficult to determine what a meaningful cutoff point is.

"Some control patients have one or two of these markers but not as many as the obstructed patients," author Charan Kumar Devarakonda, a postdoctoral fellow at UConn Health, says. "We're not testing for only one protein but rather a panel of proteins."

The team is currently working on further validation with a larger patient study for this invention. They hope to look at the validity of this panel across age, sex, and spectrum of obstruction to assess damage.

More information: Charan Kumar V.

Devarakonda et al. A novel urinary biomarker protein panel to identify children with ureteropelvic junction obstruction – A pilot study, *Journal of Pediatric Urology* (2020). [DOI: 10.1016/j.jpurol.2020.05.163](https://doi.org/10.1016/j.jpurol.2020.05.163)

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