Novel discovery could improve diagnosis and early screening of kidney stone disease

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An interdisciplinary research team led by the National University of Singapore (NUS) has recently discovered a unique panel of urine biomarkers that could accurately diagnose nephrolithiasis, also commonly known as kidney stones. These urine biomarkers may potentially be used to screen individuals at a higher risk of developing the disease. Early intervention strategies could greatly reduce the economic and social burden of the increasingly prevalent and highly recurrent disease.

Nephrolithiasis is a common ailment with a high five-year recurrence rate of 35 to 50 per cent, and can result in serious complications such as pain and chronic kidney disease. The current treatment for kidney stones employs extracorporeal shock wave lithotripsy, a non-invasive strategy that uses shock waves to fragment the kidney stones so that they can be passed out from the body. This method, while effective, has not been very successful in resolving the issue of recurrence. The increasing prevalence and high recurrence of the disease also place a substantial load on the healthcare system.

Associate Professor Eric Chan from the Department of Pharmacy at NUS Faculty of Science, in collaboration with the Department of Urology at National University Hospital (NUH), conducted a preliminary study from 2011 to 2013 to examine the underlying factors leading to the disease.

Assoc Prof Chan explained, "While diet and lifestyle choices are

believed to be among the key causes of kidney stone, the manner in which it develops remains unclear. A better understanding of the pathogenesis of the disease will facilitate the development of new, effective interventions that intercept and minimise the recurrence of the disease."

Innovative urine test to screen for kidney stone

In the preliminary study, the research team examined urine samples of 50 kidney stone patients and 50 healthy individuals over a three-year period. During which, researchers identified a group of small molecular metabolites that were found at exceptionally low concentrations in the urine samples of kidney stone patients when compared to healthy individuals.

Using the metabolites identified, the research team developed a method of diagnosing the disease with a high level of accuracy. This method is capable of giving a definitive diagnosis solely based on analysis of the urine sample as compared to current methods, which require additional diagnostic imaging for accurate diagnosis. The levels of these metabolites form a unique urinary metabolic signature for kidney stones that can potentially be used as a panel of biomarkers to screen healthy individuals who are more susceptible to developing the disease.

Researchers also noted that the differential excretion of these molecules could arise from differences in the diet, gut bacteria and liver metabolism, suggesting that kidney stone is potentially a multi-factorial disease.

Building on the findings of the preliminary study, the research team is now embarking on an in-depth clinical study to validate the group of small molecular metabolites with a secondary cohort of patients, and to further investigate the development of kidney stones. The study will

recruit 75 [kidney] [stone] patients and 75 healthy individuals to examine their diet, genes, metabolism and gut bacteria profile, as well as identify urinary biomarkers that could translate into applications for early screening and intervention. The study, termed as Disease Interception of Calcium Oxalate Nephrolithiasis (DICON), is conducted in collaboration with researchers from the Agency for Science, Technology and Research Genome Institute of Singapore and Singapore Institute of Clinical Sciences. Janssen Research & Development, LLC provided research funding for the DICON study.

"The findings from the in-depth clinical study will lay the foundation for improved interventions for the disease. The small molecular metabolites, when validated, can also be used as disease biomarkers for developing new early screening methods," added Professor Kesavan Esuvaranathan, Head of the Department of Urology at NUH.

Provided by National University of Singapore

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