**RESEARCH SYMPOSIUM PRESENTER**

**PRESENTATION TIME: 3:30 PM – 3:40 PM**

**PRESENTER: Jiun-Ruey Hu, MD, MPH (PGY1)**

**SERUM METABOLITES ARE ASSOCIATED WITH ALL-CAUSE MORTALITY IN CHRONIC KIDNEY DISEASE**

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**BACKGROUND:** Chronic kidney disease (CKD) has a high mortality rate and significant metabolic abnormalities. The levels of serum metabolites in CKD patients might provide insight into subclinical disease states and risk for future mortality. The aim of this study was to determine which serum metabolites, beyond known markers such as creatinine, reproducibly associate with long-term all-cause mortality in CKD using a rigorous discovery and replication design.

**METHODS:** We quantified metabolite levels via untargeted liquid chromatography and mass spectroscopy from serum samples of 299 subjects with CKD in the multi-center Modification of Diet in Renal Disease (MDRD) trial as a discovery cohort. We then replicated associations with mortality in 963 subjects with CKD from the multi-center African American Study of Kidney Disease and Hypertension (AASK). All regressions were carried out with adjustment for iothalamate-measured glomerular filtration rate and strict correction for multiple comparisons.

**RESULTS:** Six serum metabolites among 622 were significantly associated with mortality over a median follow-up of 17 years after adjustment for demographic and clinical covariates (p < 0.001). Three of the six metabolites identified in MDRD replicated in AASK over a median follow-up of 10 years: fumarate, allantoin, and ribonate, belonging to the energy, nucleotide, and carbohydrate pathways, respectively. Point estimates were similar in both studies and in meta-analysis (adjusted hazard ratios 1.63, 1.59, and 1.61, respectively, per doubling of the metabolite; all p values < 8.0E-05).

**CONCLUSIONS:** In conclusion, fumarate, allantoin, and ribonate were reproducibly associated with long-term all-cause mortality in CKD beyond markers of kidney function in two well characterized cohorts, providing targets for molecular investigation.

**CONTENT CATEGORY:** EPIDEMIOLOGY

**KEYWORDS:** *chronic kidney disease, metabolomics, mortality, uremic toxins*