Abstract Type : Poster exhibition
Abstract Submission No.: A-0476
Abstract Topic : Diabetic Kidney Disease + Metabolic Abnormality-related Kidney Disease

Metabolomic Profiling of Urine for Differentiating ATIN from DKD in Diabetes

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Objectives : Diabetes can lead to renal involvement in the form of diabetic kidney disease(DKD), non-diabetic kidney disease(NDKD), or both coexisting. Previous studies have reported a considerable prevalence of NDKD in diabetic patients. Differentiating NDKD from DKD in patients with diabetes is crucial, as it influences treatment strategies and prognosis. This study aims to identify metabolic biomarkers specific to NDKD, particularly acute tubular interstitial nephritis(ATIN), using metabolomics.
Methods : We included diabetic patients(n = 434) who had undergone kidney biopsy and healthy controls(n = 44) and conducted a metabolomics study analyzing 58 urine metabolites. Histopathological findings were classified into DKD alone, ATIN alone, ATIN with DKD, and other forms of NDKD, either alone or in combination with DKD. The area under the receiver operating characteristic(ROC) curve(AUC) was used to assess the diagnostic validity of differentiating ATIN from DKD in diabetic patients.
Results : Among the 434 diabetic patients, 173(40%) had DKD alone, 202(46%) had NDKD, and 59(14%) had both DKD and NDKD. Among patients with NDKD alone, 20(10%) had ATIN. Among the measured urinary metabolites, four—glycine, hippuric acid, trigonelline, and acetone—showed significant differences between the DKD-alone and ATIN-alone groups. In multivariate logistic regression analysis, elevated glycine(OR:2.672, 95% CI:1.127–6.336) and acetone levels(OR:2.939, 95% CI:1.061–8.144), as well as decreased trigonelline levels(OR:0.465, 95% CI:0.230–0.942), were associated with ATIN alone. Although the predictive power of each metabolite alone for ATIN was not significantly higher than that of eGFR plus UPCR, the combination of these metabolites demonstrated significantly higher predictive power than eGFR plus UPCR in ROC analysis.
Conclusions : This study identifies glycine, acetone, and trigonelline as promising urinary biomarkers for differentiating ATIN from DKD in diabetic patients. Their combined predictive power surpasses conventional clinical markers, highlighting their potential for improving early diagnosis and guiding more precise therapeutic strategies. Future studies are warranted to validate these findings and explore their clinical application.

THE KOREAN SOCIETY OF NEPHROLOGY

KSN SEOUL, KOREA 2025

June 19 (Thu) – 22 (Sun), 2025 Coex, Seoul, Korea

Beyond Challenges, Towards Healthier Kidney