Perbandingan Metabolit Urin pada Pasien Penyakit Ginjal Diabetes dengan Normoalbuminuria dan Albuminuria yang Mengonsumsi Metformin-Glimepirid = Comparison of Urinary Metabolites in Patients Consuming Metformin-Glimepiride with Normoalbuminuric and Albuminuria Diabetic Kidney Disease

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Abstrak

Penyakit Ginjal Diabetes (PGD) dapat menyebabkan albuminuria, yang berkembang menjadi insufisiensi ginjal. Namun, sekitar 20-40% kasus PGD merupakan PGD normoalbuminuria, yaitu gangguan fungsi ginjal dengan kadar albumin normal. Penelitian ini untuk membandingkan metabolit urin pada pasien penyakit ginjal diabetes dengan normoalbuminuria dan albuminuria yang mengonsumsi metformin-glimepirid. Desain penelitian potong lintang dengan metode consecutive sampling di Puskesmas Kecamatan Pasar Minggu dan RSUD Jati Padang. Sampel urin dan darah dikumpulkan untuk pengukuran HbA1c, UACR, dan analisis metabolit urin. Sebanyak masing-masing 16 pasien dibagi menjadi kelompok PGD normoalbuminuria dan PGD albuminuria, serta dianalisis metabolit urinnya menggunakan metabolomik tidak tertarget dengan Quadruple Time of Flight Liquid Chromatography-Mass Spectrometry. Metabolit yang berbeda signifikan divisualisasi dengan Projections to Latent Structures Discriminant Analysis (PLS-DA). Lalu, dianalisis nilai Variable Importance for the Projection (VIP) > 1.0; Fold Change (FC) >1,2 (p<0,05); dan Area Under the Receiver Operating Characteristic Curve (AUROC). Metabolit dengan nilai Area Under Curve (AUC) > 0,65 dinilai sebagai biomarker potensial. Tidak ada perbedaan bermakna pada karakteristik dasar dan klinis pada kedua kelompok, kecuali HbA1c (p<0,001). Terdapat 20 metabolit urin yang berbeda signifikan pada kelompok PGD normoalbuminuria dan albuminuria. Dari analisis jalur metabolisme pada metabolit tersebut ditemukan empat jalur metabolisme, yaitu metabolisme gliserofosfolipid, eter lipid, fenilalanin, dan triptofan. Dari keempat jalur metabolisme tersebut, ditemukan tiga metabolit biomarker potensial, yaitu glycerophosphocholine, hippuric acid, dan 2-aminobenzoic acid. Ketiga metabolit tersebut berkurang secara signifikan dari kondisi normoalbuminuria ke albuminuria. Oleh karena itu, diperlukan studi lanjut mengenai ketiga metabolit tersebut pada perkembangan PGD normoalbuminuria dan albuminuria.

.....Diabetic Kidney Disease (DKD) leads to albuminuria and gradually progresses to renal insufficiency. However, about 20-40% of DKD are normoalbuminuric DKD, which has impaired kidney function with normal albumin levels. This study compared urine metabolites in patients consuming metformin-glimepiride with normoalbuminuric and albuminuria DKD. The research design was cross-sectional with consecutive sampling method at Pasar Minggu District Public Health Centre and Jati Padang Hospital. Urine and blood samples were collected for measurement of HbA1c, UACR, and metabolite analysis. There were each 16 samples divided into normoalbuminuric DKD group and albuminuria DKD group. All subjects were analysed using non-targeted metabolomics with Quadruple Time of Flight Liquid Chromatography-Mass Spectrometry. The signature metabolites were determined by Projections to Latent Structures Discriminant Analysis (PLS-DA) with Variable Importance for the Projection (VIP) > 1.0; Fold Change (FC) >1.2 (p<0.05); and Area Under the Receiver Operating Characteristic Curve (AUROC). Metabolites with an Area

Under Curve (AUC) value > 0.65 are considered potential biomarkers. There were no significant differences in baseline and clinical characteristics of two groups, except for HbA1c ($p<0.001$). There were 20 metabolites identified between two groups. The metabolic pathway analysis of these metabolites found that four metabolic pathways were glycerophospholipid, ether lipid, phenylalanine, and tryptophan metabolism. There were three potential biomarkers, glycerophosphocholine, hippuric acid, and 2-aminobenzoic acid, enriched in these four metabolic pathways. Compared between normoalbuminuric and albuminuria groups these three metabolites were significantly reduced. Therefore, further studies are needed regarding these three metabolites in the development of normoalbuminuric and albuminuria DKD.