Kidney Injury Molecule-1 Penanda Kerusakan Tubulus Ginjal dan Kaitannya dengan Polimorfisme Gen Angiotensin Conventing Enzyme pada Penyandang Diabetes Melitus Tipe 2 = Kidney Injury Molecule-1 (KIM-1): the Indicator of Kidney Tubules Damage and Its Relationship with Polymorphism of Angiotensin Converting Enzyme Gene in Patients with Type 2 Diabetes Mellitus

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Abstrak

Patogenesis nefropati diabetik (ND) merupakan hasil interaksi faktor hemodinamik, metabolik dan lingkungan serta faktor genetik. ND biasanya tidak terdeteksi secara klinis sampai terjadi kerusakan ginjal yang bermakna dapat berupa glomerulosklerosis, tubular atrofi dan fibrosis interstitial. KIM-1 dapat digunakan sebagai penanda adanya kerusakan tubulus ginjal. Hubungan polimorfisme gen ACE dengan nefropati diabetes masih tidak konsisten.

Penelitian ini merupakan studi cross sectional komparasi antara dua kelompok penyandang DMT2 dengan atau tanpa nefropati yang bertujuan untuk mengetahui adanya kerusakan tubulus, polimorfisme gen ACE dan menganalisis hubungannya dengan kadar KIM-1 terhadap terjadinya kelainan tubulus. Didapatkan adanya peningkatan ekskresi KIM-1 urin pada 19 subjek pre-nefropati dengan median 1,3 (interquartile 1,5) ng/mL, 25 subjek nefropati insipien dengan median 1,6 (interquartile 2,3) ng/mL dan 12 subjek nefropati overt dengan rerata kadar KIM-1 3,1 ± 2,4 ng/mL. Terdapat polimorfisme gen ACE pada penyandang DMT2. Proporsi genotipe DD 9,3%, ID 33,3% dan II 57,4% pada kelompok NND, pada kelompok ND proporsi genotipe DD 4,7%, ID 34,1% dan genotipe II 61,2%.

Dijumpai adanya hubungan bermakna antara alel D dengan peningkatan ekskresi KIM-1 urin pada kelompok pre-nefropati (p = 0,030). Peningkatan kadar KIM-1 urin pada kelompok pre-nefropati menunjukkan adanya kerusakan tubulus yang merupakan proses awal nefropati DM. Distribusi genotipe polimorfisme gen ACE pada penelitian ini menyerupai penelitian lain di negara-negara Asia, sedangkan di negara Eropa genotipe DD lebih banyak daripada genotipe II. Hubungan bermakna alel D dengan kadar KIM-1 hanya pada kelompok prenefropati mungkin disebabkan adanya faktor lain seperti kadar glukosa, kontrol glikemik, ureum, kreatinin dan kadar trigliserida yang memengaruhi.

Simpulan: Terdapat peningkatan ekskresi KIM-1 urin pada penyandang DMT2 kelompok pre-nefropati yang meningkat secara bermakna pada penyandang DMT2 dengan nefropati overt. Peningkatan ekskresi KIM-1 urin dapat dipakai sebagai penanda kerusakan tubulus. Terdapat polimofisme gen ACE pada penyandang DMT2. Genotipe II lebih banyak dibanding genotipe ID dan DD. Dijumpai adanya hubungan alel D dengan peningkatan kadar KIM-1 urin pada penyandang DMT2 pre-nefropati.

.....The pathogenesis of nephropathy diabetic (ND) is the result of the interaction of haemodynamic, metabolic, environment, and genetic factors. In general, ND was clinically undetectable until kidney has been damaged significantly, in the form of glomerulosclerosis, tubular atrophy, or interstitial fibrosis. KIM-1 can be used as the initial indicator of kidney tubules damage. The relationship between ACE gene polymorphism and diabetic nephropathy was still inconsistent.

This research was a comparative cross-sectional study on two groups of DMT2 patients with and without

nephropathy diabetic. The objectives of this study were to identify the tubules damage, ACE gene polymorphism, and to analyze the relationship between the degree of KIM-1 and the tubules damage. The increase of KIM-1 urine excretion was found in 19 pre-nephropathy subject (median = 1.3 with interquartile 1.5 ng/mL), in 25 incipient nephropathy subject (median = 1.6 (2.3) ng/mL), in 12 overt nephropathy subject (Mean = 3.1 ± 2,4 ng/mL). ACE polymorphism gene was found in DMT2 patients. In the NDD group, the genotype proportion of DD = 9.3%, ID = 33.3% and II = 57.4%. Whereas, in the ND group, the figures were 4.7%, 34.1% and 61.2%, respectively.

Significant relationship was found between allele D and the increase of KIM-1 urine on pre-nephropathy group ($p = 0.030$). The increase of KIM-1 urine on prenephropathy group shows the tubules damage which is the initial process of nephropathy diabetic. The genotype distribution of ACE gene polymorphism in this study was similar with the studies in Asian countries; however, in European countries the genotype DD is found higher than genotype II. The significant relationship between allele D and KIM-1 level in pre-nephropathy group might be the influence of other factors, such as glucose level, glycaemic control, urea, creatinine, and triglyceride level.

Conclusion: There was KIM-1 excretion increased on DMT2 pre-nephropathy group, which increase significantly in DMT2 overt nephropathy group. The increase of KIM-1 urine excretion can be used as the indicator of tubules damage. ACE gene polymorphism was found in DMT2 group, with genotype II was higher than genotype ID and DD. A significant relationship between allele D and the increase of KIM-1 urine excretion was found in pre-nephropathy group.