

Faktor-Faktor yang Berpengaruh terhadap Kejadian Batu Ginjal: Kajian Berdasarkan Faktor Polimorfisme Gen CaSR, CLDN14, VDR, ALPL, Ekspresi Sitokin Inflamasi, Klinis, dan Demografi = Kidney Stones Formation Factors: A Study Based on Gene Polymorphism Factor of CaSR, CLDN 14, VDR, ALPL, Inflammation Cytokine Expression, Clinical, and Demography Factors

Widi Atmoko, author

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Abstrak

Batu ginjal merupakan salah satu penyakit urologi tersering di Indonesia dan dipengaruhi oleh berbagai faktor inflamasi, faktor klinis dan demografi, namun, 50% faktor predisposisi batu ginjal diketahui juga dipengaruhi oleh faktor genetik. Namun, sampai saat ini, belum ada studi yang menganalisis faktor risiko kejadian batu ginjal dari segi polimorfisme gen, sitokin inflamasi, klinis, dan demografi secara komprehensif, serta belum diketahui mekanisme keseluruhan faktor-faktor tersebut dalam menyebabkan batu ginjal. Oleh sebab itu, penelitian ini dibuat untuk menjelaskan mekanisme faktor risiko tersebut terhadap kejadian batu ginjal sebagai pencegahan terjadinya batu ginjal. Penelitian dilakukan di RSUPN Dr. Cipto Mangunkusumo dengan desain kasus kontrol sejak Maret 2021 hingga Maret 2024 dengan jumlah 308 subjek, yaitu 154 subjek kelompok kasus dan 154 subjek kelompok kontrol sehat. Pada setiap pasien dilakukan pencatatan dan evaluasi terhadap data demografi, pemeriksaan biokimia dan polimorfisme genetik dievaluasi dari sampel darah, ekspresi gen sitokin inflamasi dan urinalisis dari sampel urin pagi, serta pemeriksaan urin 24 jam. Asupan cairan dinilai menggunakan kuesioner Liq-In7. Analisis bivariat dan multivariat dilakukan menggunakan SPSS versi 20 sedangkan analisis jalur dilakukan menggunakan JASP 0.19.1.0. Dari penelitian didapatkan usia lebih tua, peningkatan kadar kreatinin darah, peningkatan kadar kalsium urin, kondisi ISK, genotipe GT gen CaSR rs1801725, genotipe CT gen CLDN14 rs219780, genotipe AG dan GG gen VDR rs2228570, genotipe CT gen VDR rs1544410, dan genotipe CT gen ALPL rs1256328 berhubungan dengan peningkatan risiko kejadian batu ginjal. Peningkatan kadar sitrat urin dan genotipe AG gen CaSR rs1042636 menurunkan risiko batu ginjal. Selain itu, rerata asupan cairan lebih rendah, asam urat urin lebih rendah, asam urat serum lebih tinggi, dan proporsi Genotipe CT gen VDR rs731236 dan pekerja kantor lebih rendah didapatkan pada kelompok kasus secara bermakna, namun tidak termasuk dalam faktor risiko independen berdasarkan hasil multivariat. Upregulation ekspresi IL-8 juga didapatkan pada kelompok kasus. Pada analisis jalur, varian gen VDR rs2228570, CLDN14 rs219780, CaSR rs1801725, kreatinin serum, dan usia lebih dominan memiliki efek positif langsung terhadap batu ginjal. Di sisi lain, varian gen VDR rs1544410 memiliki efek positif tidak langsung yang lebih dominan terhadap batu ginjal melalui kalsium urin. Prediktor batu ginjal dengan sistem skoring menggunakan beberapa variabel telah dikembangkan dengan sensitivitas dan spesifisitas yang baik. Dengan mengidentifikasi faktor risiko terkait batu ginjal yang dapat dan tidak dapat dimodifikasi bisa menjadi target utama dalam pencegahan primer batu ginjal.

.....Kidney stones are among the most common urological diseases in Indonesia, influenced by various inflammatory, clinical, and demographic factors, but 50% of the predisposition is also attributed to genetic factors. To date, no comprehensive studies have analyzed kidney stone risk factors by considering genetic

polymorphisms, inflammatory cytokines, clinical, and demographics factors. Moreover, the comprehensive mechanisms by which these risk factors contribute to kidney stone formation remain unclear. Therefore, this study was conducted to elucidate how these risk factors contribute to kidney stone occurrence, aiming to prevent kidney stones. The study was conducted at Dr. Cipto Mangunkusumo Hospital using a case-control design from March 2021 to March 2024, involving 308 subjects, comprising 154 cases and 154 healthy controls. Demographic data were collected through subject interviews. Biochemical and genetic polymorphism analyses were performed using blood samples, while inflammatory cytokine gene expression and urinalysis were evaluated from morning urine samples. Twenty-four-hour urine samples were utilized to analyze the levels of dissolved molecules and urine pH. Fluid intake was assessed using the Liq-In7 questionnaire. Bivariate and multivariate analysis was conducted using SPSS version 20, whereas path analysis was performed using JASP 0.19.1.0. The study identified that older age, increased serum creatinine levels, increased urinary calcium levels, urinary tract infections, the GT genotype of the CaSR rs1801725 gene, the CT genotype of the CLDN14 rs219780, the AG and GG genotypes of the VDR rs2228570, the CT genotype of the VDR rs1544410, and the CT genotype of the ALPL rs1256328 were associated with an increased risk of kidney stone. In contrast, higher urinary citrate levels and the AG genotype of the CaSR rs1042636 gene were associated with a reduced risk of kidney stones. Furthermore, the case group showed significantly lower mean fluid intake, lower urinary uric acid levels, higher serum uric acid levels, and a lower proportion of the CT genotype of the VDR rs731236 gene and office workers. However, these variables were not identified as independent risk factors based on multivariate analysis. IL-8 expression was also observed to be upregulated in the case group. Path analysis revealed that the VDR rs2228570, CLDN14 rs219780, and CaSR rs1801725 genetic variants, serum creatinine, and age, predominantly exerted direct positive effects on kidney stone. Conversely, the VDR rs1544410 genetic variant had a more pronounced indirect positive effect through urinary calcium levels. Scoring systems for kidney stone prediction, incorporating these variables, had been developed with good sensitivity and specificity. Identifying modifiable and non-modifiable risk factors related to kidney stones could serve as critical targets for primary prevention strategies.