

Analisis mutasi gen Dihydrofolate Reductase (dfr) dan Dihydropteroate Synthase (sul) pada *Escherichia coli* dari infeksi saluran kemih dengan fenotip Resistan Trimetoprim-Sulfametoksazol = Mutation analysis of the dihydrofolate reductase (dfr) and dihydropteroate synthase (sul) genes in *E. coli* isolated from the urinary tract with a trimethoprim-sulfamethoxazole resistant phenotype

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Abstrak

Trimetoprim-sulfametoksazol (TMP/SMX) merupakan golongan antibiotik lini pertama yang digunakan untuk pengobatan infeksi saluran kemih. Antibiotik TMP/SMX bekerja dengan menghambat reaksi enzimatik sintesis folat bakteri pada dua tahap yang berurutan pada bakteri, sehingga kombinasi obat ini dapat memberikan efek sinergi. Gen *dfr* dan gen *sul* merupakan gen yang mengkode DHFR dan DHPS yang terdapat di Mobile Genetic Element (MGE) yang keberadaannya dapat meningkatkan kejadian resistensi bakteri terhadap antibiotik trimetoprim-sulfametoksazol. 8 isolat *Escherichia coli* diketahui resistensi terhadap trimetoprim-sulfametoksazol secara fenotipik diperiksa keberadaan MGE *dfr1*, *dfr5*, *dfr7&17*, *sul1* dan *sul2* melalui metode PCR konvensional, dilanjutkan dengan analisis asam amino untuk melihat ada atau tidaknya mutasi. 7 dari 8 isolat *Escherichia coli* yang resistensi antibiotik trimetoprim-sulfametoksazol memiliki MGE *dfr* dan *sul* yang berkesesuaian dengan fenotipik resistensi trimetoprim-sulfametoksazol. Mutasi asam amino dijumpai pada gen *dfr1* isolat no 95 pada posisi I55V; D64S; N65D; I70V; N129S. *dfr5* Isolat nomor 14, 53, 88 dan 95 memiliki jumlah mutasi asam amino sebanyak 10 titik pada posisi: A17G; A20S; D21N; N22D; I26V; P29Q; Y36D; Y37D; L41F; D43G. sedangkan gen *sul2* isolat 14, 29, 78, 79 dan 88 mutasi pada posisi G8W dan I12M. Keberadaan MGE *dfr* dan *sul* pada isolat klinis menunjukkan adanya mekanisme resistensi ekstrinsik bakteri yang memerlukan perhatian khusus terhadap peningkatan kejadian resistensi bakteri.

.....Trimethoprim-sulfamethoxazole (TMP/SMX) is a class of first-line antibiotics used for the treatment of urinary tract infections. TMP/SMX antibiotics work by inhibiting the enzymatic reaction of bacterial folate synthesis at two successive stages in bacteria, so that this drug combination can provide a synergistic effect. The *dfr* gene and *sul* gene are genes that code for DHFR and DHPS found in the Mobile Genetic Element (MGE) whose presence can increase the incidence of bacterial resistance to the antibiotic trimethoprim-sulfamethoxazole. 8 isolates of *Escherichia coli* known to be resistant to trimethoprim-sulfamethoxazole phenotypically examined for the presence of MGE *dfr1*, *dfr5*, *dfr7&17*, *sul1* and *sul2* through conventional PCR methods, followed by amino acid analysis to see the presence or absence of mutations. 7 of the 8 isolates of *Escherichia coli* that were trimethoprim-sulfamethoxazole antibiotic retention had MGE *dfr* and *sul* corresponding to the phenotypic resistance of trimethoprim-sulfamethoxazole. Amino acid mutations were found in the *dfr1* gene isolate no 95 at position I55V; D64S; N65D; I70V; N129S. *dfr5* Isolates number 14, 53, 88 and 95 have a number of amino acid mutations of 10 points at position: A17G; A20S; D21N; N22D; I26V; P29Q; Y36D; Y37D; L41F; D43G. while the *sul2* gene isolates 14, 29, 78, 79 and 88 mutations at the G8W and I12M positions. The presence of MGE *dfr* and *sul* in clinical isolates suggests the existence of a mechanism of bacterial extrinsic resistance that requires special attention to the increased

incidence of bacterial resistance.