Karakterisasi Molekuler gen gyrA dan gyrB pada Quinolone Resistance Determining Region (QRDR) Escherichia coli Resisten Ciprofloxacin yang Diisolasi dari Isolat Klinis Pasien Infeksi Saluran Kemih (ISK) = Molecular Characterization of gyrA and gyrB Genes on Quinolone Resistance Determining Region (QRDR) Ciprofloxacin Resistant Escherichia coli Isolated from Clinical Isolates of Urinary Tract Infection (UTI) Patients

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Abstrak

Escherichia coli bertanggung jawab atas 80-90% menyebabkan infeksi saluran kemih (ISK). Ciprofloxacin merupakan salah satu antibiotik yang berspektrum luas yang bekerja efektif terhadap E. coli yang biasa digunakan dalam pengobatan ISK. Namun telah banyak dilaporkan meningkatnya resistensi E. coli penyebab ISK terhadap Ciprofloxacin. Mutasi pada QRDR gen gyrA dan gyrB merupakan 2 gen yang banyak dilaporkan sebagai penyebab resitesnsi terhadap Ciprofloxacin. Di Indonesia, studi mutasi gen gyrA dan gyrB yang dikaitkan dengan resistensi E. coli penyebab ISK terhadap Ciprofloxacin belum dilaporkan. Oleh karena itu, dalam penelitian ini dilakukan karakterisasi daerah QRDR gen gyrA dan gyrB menggunakan metoda PCR dan DNA sekuensing yang mencakup posisi asam amino 40-110 (gyrA) dan posisi 407-473 (gyrB). Untuk gen gyrA, dari semua isolat (9 isolat) mengalami 2 perubahan asam amino pada posisi 83 (S83L) dan 87 (D87N) di daerah QRDR. 1 isolat mengalami 2 tambahan perubahan asam amino diluar daerah QRDR pada posisi asam amino 55 (L55V) dan posisi asam amino 66 (S66T). Adapun gen gyrB, dari 9 isolat semua isolat tidak mengalami perubahan asam amino di daerah QRDR. Berdasarkan analisis docking, isolat yang mengalami 4 perubahan asam amino (gyrA) menunjukkan pelemahan afinitas yang kuat antara DNA gyrase dan ciprofloxacin dibandingkan dengan isolat yang hanya mengalami 2 perubahan asam amino pada daerah QRDR.

.....Escherichia coli is responsible for 80-90% of causes of urinary tract infections (UTI). Ciprofloxacin is broad spectrum antibiotic that works effectively against E. coli which is commonly used in the treatment of UTI. However, there have been many reports of increasing resistance of E. coli that causes UTI to Ciprofloxacin. Mutations in the QRDR genes gyrA and gyrB are two genes that have been widely reported as causes of resistance to Ciprofloxacin. In Indonesia, studies of gyrA and gyrB gene mutations associated with resistance of UTI-causing E. coli to Ciprofloxacin have not been reported. Therefore, in this study, the QRDR region of the gyrA and gyrB genes was characterized using PCR and DNA sequencing methods covering amino acid positions 40-110 (gyrA) and positions 407-473 (gyrB). For the gyrA gene, all isolates (9 isolates) experienced 2 amino acid changes at positions 83 (S83L) and 87 (D87N) in the QRDR region. 1 isolate experienced 2 additional amino acid changes outside the QRDR region at amino acid position 55 (L55V) and amino acid position 66 (S66T). As for the gyrB gene, of the 9 isolates, all isolates did not experience amino acid changes in the QRDR region. Based on docking analysis, isolates that experienced 4 amino acid changes (gyrA) showed a strong weakening of the affinity between DNA gyrase and ciprofloxacin compared to isolates that only experienced 2 amino acid changes in the QRDR region.