

## ABSTRAK

### VARIASI GENETIK GEN *folA* dan *folP* SEBAGAI MARKER RESISTENSI COTRIMOXAZOL PADA *Streptococcus pneumoniae*

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*Streptococcus pneumoniae* adalah bakteri penyebab utama penyakit pneumonia, meningitis, bakteremia dan sepsis di seluruh dunia. Penanganan dengan antibiotik telah memunculkan kasus-kasus resistensi terhadap antibiotik, salah satunya adalah Cotrimoxazol / Trimetoprim-Sulfametoxazol (CTX). Resistensi terhadap Trimetoprim maupun Sulfametoxazol dapat terjadi karena mutasi *non-synonymous* pada gen-gen pengkode enzim target, yaitu gen *folA* (pengkode DHFR) dan *folP* (pengkode DHPS). Penelitian ini dilakukan pada Januari-Juni 2016. Sebanyak 51 isolat *Streptococcus pneumoniae* dari arsip sebuah *carriage study* di Lombok, Indonesia, diuji suseptibilitasnya terhadap panel antibiotik dan diukur *Minimum Inhibitory Concentration* (MIC) terhadap CTX. Isolasi DNA dilanjutkan dengan amplifikasi gen *folA* dan *folP* dengan PCR lalu di-sekuensing. Data sekuens dianalisis dengan menggunakan *BioEdit* untuk keperluan analisis mutasional dan filogenetik, sehingga didapatkan asosiasi antara SNP pada gen *folA* dan gen *folP*. Hasil analisis filogenetik menunjukkan bahwa SNP acak pada *folA* berkorelasi dengan resistensi terhadap CTX, tetapi tidak pada *folP*. Hasil analisis mutasional menunjukkan bahwa genotipe Asp-92-Ala Ile-100-Leu pada DHFR dan genotipe STRPRPGSSYVEIE pada DHPS berkorelasi tinggi dengan resistensi terhadap CTX.

Kata kunci: *S. pneumoniae* resisten CTX, gen *folA* dan *folP*, protein DHFR dan DHPS, nsSNP, marker resistensi

## ABSTRACT

### GENETIC VARIATION OF *folA* AND *folP* GENE AS RESISTANCE MARKERS AGAINST COTRIMOXAZOLE IN *Streptococcus pneumoniae*

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*Streptococcus pneumoniae* is the common cause of bacterial pneumonia, meningitis, bacteremia and sepsis around the world. The use of antibiotics, such as Cotrimoxazole (Trimethoprim-Sulfamethoxazole) had lead antibiotic resistance cases. Both Trimethoprim and Sulfamethoxazole resistance caused by *non-synonymous* mutation in the target enzyme of the both antibiotics, DHFR and DHPS, encoded by *folA* and *folP* gene. This study was held by January-June 2016. A 51 of *S. pneumoniae* archive isolates from a carriage study in Lombok were tested their susceptibility against panel of antibiotics and Minimum Inhibitory Concentration (MIC) against CTX. DNA isolation are followed by PCR and Sequencing of *folA* and *folP* gene. Sequence of *folA* and *folP* gene that obtained were analysed by BioEdit for mutational and phylogenetics analysis. Phylogenetic analysis result shows that random SNPs in *folA* correlated with CTX resistance, but not in *folP*. Mutational analysis result shows that variation Asp-92-Ala Ile-100-Leu from DHFR and variation STRPRPGSSYVEIE of DHPS are correlated with CTX resistance in *S. pneumoniae* in Indonesia, so that the variations can be used as CTX-resistance marker in *S. pneumoniae*.

Keywords: CTX resistant *S. pneumoniae*, *folA* and *folP* gene, DHFR and DHPS protein, nsSNP, resistance marker