

Karakterisasi Molekuler Gen S1 dan Patogenisitas Isolat Virus Varian *Infectious Bronchitis* asal Ayam Komersial Tahun 2017-2023

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INTISARI

Penyakit *Infectious Bronchitis* menjadi ancaman industri perunggasan komersial Indonesia, ditandai dengan penurunan produksi dan munculnya kasus dari unggas yang sudah divaksinasi. Rendahnya efektivitas proteksi dari vaksin konvensional terhadap varian yang beredar memicu kebutuhan mendesak untuk memahami dinamika virulensi virus lokal. Penelitian ini bertujuan mengkaji secara komprehensif karakteristik molekuler dan patogenisitas *in vivo* isolat IBV (asal broiler, layer, *breeder*) varian lokal Indonesia tahun 2017–2023. Penelitian dilakukan di Universitas Gadjah Mada. Sebanyak 14 isolat IBV GI-19 asal kasus lapangan periode 2017–2023 telah dikarakterisasi secara molekuler pada fragmen gen S1, dilanjutkan deteksi gen S1 utuh dengan RT-PCR, dianalisis karakterisasi molekuler S1 utuh dengan MEGA-X, dan patogenisitas *in vivo*. Metode yang digunakan meliputi RT-PCR S1 utuh, analisis filogenetik gen S1 utuh untuk *genotyping*, studi mutasi dan jarak genetik pada situs fungsional S1, serta imunoinformatika yang mencakup prediksi epitop sel B dan T dan *docking* RNA S1-TLR (TLR3 dan TLR7). Uji patogenisitas *in vivo* dilakukan dengan infeksi buatan IBV pada ayam *specific antibody negative* dengan fokus pada kinetika *viral load*, respon interferon (α , β , γ), dan pola lesi histopatologi akut (1, 5, dan 10 hari pasca infeksi) hingga kronis (16 minggu pasca infeksi) pada organ ginjal, jantung, dan reproduksi. Hasil analisis didapat temuan bahwa isolat ke dalam dua sub-genotipe INAQX-1 dan INAQX-2, mengindikasikan jarak genetik intra-genotipe 1,7-4,6% pada S1, serta mutasi khas pada *receptor binding domain* dan *cleavage site*. Sub-genotipe INAQX-2 teridentifikasi memiliki komposisi epitop yang lebih luas (91% epitop sel T-helper dan 85% epitop sel T-sitotoksik), serta memicu respon interferon (IFN) dengan diikuti penurunan *viral load* yang merupakan indikasi netralisasi virus. Kedua sub-genotipe terbukti bersifat nefrotropisme dengan menyebabkan nefrosis tubuler dan proliferasi sel mesangial persisten; menyebabkan lesi pada organ reproduksi ovarium dan oviduk; serta kardiotropisme yang belum pernah dilaporkan sebelumnya. Kesimpulan penelitian ini teramati adanya variasi intra-genotipe IBV lokal pada tingkat molekuler, yang diikuti dengan perbedaan patogenisitasnya.

Kata kunci : Karakterisasi molekuler, patogenisitas, glikoprotein *spike* 1, virus *infectious bronchitis*, varian

Molecular Characterization of S1 Gene and Pathogenicity of *Infectious Bronchitis* Varian Virus Isolates from Commercial Chicken in 2017-2023

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ABSTRACT

Infectious Bronchitis disease is a challenge to Indonesia's commercial poultry industry, marked by a decrease in production and the emergence of cases of vaccinated poultry. The low protective effectiveness of conventional vaccines against circulating variants triggers an urgent need to understand the dynamics of local viral virulence. This study aims to comprehensively examine the molecular characteristics and pathogenicity of local variant of Indonesian IBV isolates in 2017–2023. The research was conducted at the Universitas Gadjah Mada. A total of 14 IBV GI-19 isolates from field cases for the 2017–2023 period have been molecularly characterized on S1 gene fragments, analyzed for full gene of S1 molecular characterization and pathogenicity *in vivo*. The methods used include S1 RT-PCR, phylogenetic analysis of full S1 gene for genotyping, mutation and genetic distance studies at S1 functional sites, and immunoinformatics which include B and T cell epitope prediction and S1-TLR RNA *docking* (TLR3 and TLR7). *In vivo* pathogenicity testing was performed with IBV artificial infection in chickens specific antibody negative with a focus on *viral load* kinetics, interferon response (α , β , γ), and acute histopathological lesion patterns (1, 5, and 10 days post-infection) to chronic (16 weeks post-infection) in kidney, heart, and reproductive organs. The results of the analysis were found that the isolates into two sub-genotypes, INAQX-1 and INAQX-2, indicated an intra-genotype genetic distance of 1.7-4.6% in S1, as well as typical mutations in the receptor binding domain and cleavage site. The INAQX-2 sub-genotype was indicated to have a broader epitope composition and trigger a better interferon response (IFN), predicted in more efficient neutralization of the virus than INAQX-1. Both sub-genotypes have been shown to be nephrotropism by causing tubular nephrosis and persistent mesangial cell proliferation; causing lesions of the reproductive organs of the ovaries and oviducts; as well as previously reported cardiotropism. The conclusion of this study is that there is intra-genotype variation of local IBV at the molecular level, which is followed by differences in pathogenicity. The main suggestion is the development of a specific homologous vaccine of the INAQX sub-genotype by utilizing the immunogenic data of this study, to overcome the failure of vaccination protection in the field.

Keywords : Molecular characterization, pathogenicity, *spike* glycoprotein 1, infectious bronchitis virus, variant