Association between arg753gln and arg677trp polymorphisms of tlr2 gene with active pulmonary tuberculosis in an Indonesian population

Arto Yuwono Soeroto, author

Abstrak

Background: Toll-like receptor is a pattern recognition receptor (PRR) that recognize pathogen-associated molecular pattern (PAMP) in a microorganism. Macrophages recognize the presence of mycobacteria through Toll-Like Receptor 2 (TLR2) and signaling further lead to the production of cytokines, both proinflammatory TNF-, IL-1, IL-6, IL-12, IL-15, IL-18 and IFN-, as well as anti-inflammatory IL4, IL-10 and TGF-. TLR2 gene polymorphism is strongly determined by ethnicity and geography. Therefore it is necessary to uncovered the existence and association between Arg753Gln and Arg677Trp TLR2 gene polymorphism with TB susceptibility and its underlying mechanisms in Indonesian population in Bandung West Java.
Methods: analytical observational study with cross-sectional design was conducted in Hasan Sadikin General Hospital Bandung from April 2011 to May 2012. Study population consisted of active pulmonary TB patient with positive AFB smear and Latent TB to ascertain previous MTb exposure. Polymorphism of gen Arg753Gln and Arg677Trp gene was determined with polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) methods. Plasma levels of IFN-, TNF-, IL-10 and IL-12 were also compared between active and latent TB group.
Results: heterozygote Arg753Gln TLR2 gene polymorphism was found in 9 of 86 pulmonary TB subjects (10.5%) but none in the latent TB group. The Arg677Trp polymorphism was not found in both groups. The odds ratio for Arg753Gln existence was 28.07 (p=0.022). No differences in the levels of IFN-, TNF-, IL-10 and IL-12 between active pulmonary TB and latent TB subjects with and without Arg753Gln TLR2 gene polymorphism.
Conlusion: Arg753Gln polymorphism of TLR2 gene is a risk factor for active pulmonary TB while Arg677Trp polymorphism is not. The Increased risk is not mediated by the difference in IFN-, TNF-, IL-10 and IL-12 serum levels.
.....Latar belakang: Toll-like receptor (TLR) adalah reseptor pengenalan pola yang mengenali pola molekul terkait patogen dalam mikroorganisme. Makrofag mengenali adanya mikobakteri melalui Toll-Like Receptor 2 (TLR2) dan penanda lanjutan pada produksi sitokin, proinflammatory TNF-, IL-1, IL-6, IL-12, IL-15, IL-18 dan IFN-, serta anti-inflamasi IL4, IL-10 dan TGF-. Polimorfisme gen TLR2 sangat ditentukan oleh etnisitas dan geografi, karenanya diperlukan analisis hubungan polimorfisme Arg753Gln dan Arg677Trp gen TLR2 dengan kerentanan menderita TB paru aktif dan peranan beberapa sitokin pada populasi Indonesia di Bandung Jawa Barat.
Metode: penelitian observasional analitik dengan rancangan potong lintang dilaksanakan pada periode April 2011–Mei 2012 di RS Dr. Hasan Sadikin Bandung. Populasi penelitian terdiri dari penderita TB paru aktif dengan BTA positif dan sebagai pembanding adalah TB laten. Adanya polimorfisme gen Arg753Gln dan Arg677Trp diperiksa dengan metode polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Kadar sitokin IFN-, TNF-, IL-10, dan IL-12 juga dibandingkan antara kelompok TB aktif dan

TB laten.
Hasil: polimorfisme heterozigot Arg753Gln gen TLR2 ditemukan pada 9 dari 86 (10.5%) penderita TB paru aktif dan tidak ditemukan pada TB laten. Pada kedua kelompok tidak ditemukan polimorfisme Arg677Trp. Odds Ratio untuk polimorfisme Arg753Gln adalah 28,07 (p=0,022). Tidak ditemukan perbedaan bermakna kadar sitokin IFN-, TNF-, IL-10, dan IL-12 antara penderita TB paru dengan polimorfisme Arg753Gln dan penderita TB paru tanpa polimorfisme tersebut.
Kesimpulan: polimorfisme Arg753Gln gen TLR2 merupakan faktor risiko menderita TB paru pada populasi orang Indonesia di Bandung, sedangkan polimorfisme Arg677Trp gen TLR2 bukan. Peningkatan risiko ini tidak terkait dengan perubahan kadar IFN-, TNF-, IL-10 maupun IL-12.