# The role of Cytotoxic T-lymphocyte-associated Protein 4 (CTLA-4) Gene, Thyroid Stimulating Hormone Receptor (TSHR) Gene and Regulatory T-cells as risk factors for relapse in patients with graves disease

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Abstrak

Background: graves disease (GD) is the most common condition of thyrotoxicosis. The management of GD is initiated with the administration of antithyroid drugs; however, it requires a long time to achieve remission. In reality more than 50% of patients who had remission may be at risk for relapse after the drug is stopped. This study aimed to evaluate the role of clinical factors such as smoking habit, degree of ophtalmopathy, degree of thyroid enlargement; genetic factors such as CTLA 4 gene on nucleotide 49 at codon 17 of exon 1, CTLA 4 gene of promotor -318, TSHR gene polymorphism rs2268458 of intron 1; and immunological factors such as regulatory T cells (Treg) and thyroid receptor antibody (TRAb); that affecting the relapse of patients with Graves disease in Indonesia. Methods: this was a case control study, that compared 72 subjects who had relapse and 72 subjects without relapse at 12 months after cessation of antithyroid treatment, who met the inclusion criteria. Genetic polymorphism examination was performed using PCR-RFLP. The number of regulatory T cells was counted using flow cytometry analysis and ELISA was used to measure TRAb. The logistic regression was used since the dependent variables were categorical variables. Results: the analysis of this study demonstrated that there was a correlation between relapse of disease and family factors (p=0.008), age at diagnosis (p=0.021), 2nd degree of Graves ophthalmopathy (p=0.001), enlarged thyroid gland, which exceeded the lateral edge of the sternocleidomastoid muscles (p=0.040), duration of remission period (p=0.029), GG genotype of CTLA 4 gene on the nucleotide 49 at codon 17 of exon 1 (p=0.016), CC genotype of TSHR gene on the rs2268458 of intron 1 (p=0.003), the number of regulatory T cells (p=0.001) and TRAb levels (p=0.002). Conclusion: genetic polymorphisms of CTLA 4 gene on the nucleotide 49 at codon 17 of exon 1, TSHR gene SNP rs2268458 of intron 1, number of regulatory T cells and TRAb levels play a role as risk factors for relapse in patients with Graves disease.