

ABSTRACT

Background : studies on the relation between RSV bronchiolitis in infancy and subsequent development of clinical asthma have shown different results : some investigator have found a connection whereas others have not. HLA class II genetic polymorphism has not been implicated in susceptibility to specific immune responsiveness to respiratory syncytial virus (RSV) antigens, and may also influence the development of asthma. To determine the predictive value of these polymorphisms we have assessed their Odd's Ratio and *p* level for the development of asthma that is being followed longitudinally from suffering RSV bronchiolitis. Until now, no study have been reported that the genotype of HLA-DRB1* were associated with asthma after RSV bronchiolitis and no Indonesian study have reported that the genotype of HLA-DRB1* were associated with asthma phenotype.

Objective : In order to assess accurately the influence of HLA-DRB1* genotype in the immune response, we typed 82 patients with asthma after RSV bronchiolitis, asthma after non RSV bronchiolitis, non asthmatic RSV bronchiolitis, non asthmatic non RSV bronchiolitis and healthy control subjects.

Methods : Each individual was fully typed for HLA-DRB1* genotype using a combination of sequence-specific oligonucleotide probes (SSOP) and polymerase chain reaction (PCR) typing. The

diagnoses of RSV bronchiolitis verified using the Abbot test pack RSV, a rapid enzyme immuno assay for direct detection of viral antigen in nasopharyngeal secretion. All children reported for the follow up, which included physical examination, changes in FEV1 were determined using spirometry, total serum IgE, IL-4, IFN- γ were determined using the enzyme-linked immunosorbant assay (Elisa) method, ThCD4⁺ and TcCD8⁺ were determined using immunohistochemistry staining.

Results : using appropriate statistical test, significant allelic associations were found between HLA-DRB1*07 (OR=11.65 , $p=0.008$), HLA-DRB1*07-DRB4 (OR=13.74 , $p = 0.012$) haplotype and asthma after RSV bronchiolitis compared to non asthma RSV bronchiolitis, HLA-DRB1*07 (OR=35.92 , $p = 0.003$), HLA-DRB1*07-DRB4 (OR=77.0 , $p = 0.007$) and asthma phenotype compared to non asthmatic patients. On the other hand, HLA-DRB1*03, HLA-DRB1*03-DRB3, HLA-DRB1*12-DRB3, HLA-DRB1*15-DRB5 and HLA-DRB1*15 after RSV bronchiolitis, HLA-DRB1*03, HLA-DRB1*03-DRB3, HLA-DRB1*12-DRB3, and HLA-DRB1*13 were negatively associated with asthma. Furthermore, HLA-DRB1*07 haplotype tended to be mild acute episode of asthma attack.

Conclusions : These results confirm association between HLA-DRB1*07 , HLA-DRB1*07-DRB4 haplotype and asthma after bronchiolitis RSV and HLA-DRB1*07 genotype tended to be mild. Furthermore, the HLA-DRB1*07 haplotype as asthma genotype was

demonstrated, and suggest that HLA class II restriction play a critical role in the development of the asthma and asthma after RSV bronchiolitis.

Key words: Asthma after bronciolitis RSV, HLA-DRB1*, ThCD4+, TcCD8+, IgE, Eosinophil, IL-4, IFN- γ , FEV-1.

