Association of JAK2 gene polymorphisms in Malaysian patients with Crohn’s disease

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Abstract

Crohn’s disease (CD) is one of the prominent subtypes of inflammatory bowel disease (IBD). It affects any part of the gastrointestinal (GI) tract, especially colon and ileum. CD is on a rising trend in Asia, with prevalence of 26 cases per 100,000 population in Malaysia. To date, there is no cure available for CD. Although the exact cause of CD remains ambiguous, genetic factor has been shown to play a very important role in the development of CD. Janus kinase 2 (JAK2) is the key protein in JAK/STAT signalling pathway that regulates inflammatory response in mucosal barrier. Alteration of the JAK2 protein due to the changes in its gene could lead to unregulated inflammations that result in the onset of CD. Thus, we aim to study the association of JAK2 gene polymorphisms in Malaysian CD patients. A total of 99 CD patients and 297 matching controls were recruited from University Malaya Medical Centre. Venous blood was drawn and genomic DNA was extracted via a conventional phenol-chloroform extraction method. A total of four selected JAK2 SNPs (rs10758669, rs7849191, rs10974944, and rs10975003) were typed via TaqMan® SNP genotyping assays in a real-time PCR system. Genotyping results were validated by PCR-resequencing approach. Genomic and allelic data were tabulated and analyzed using statistical tests to associate the SNPs with the onset of CD in Malaysian population. None of the four SNPs showed significant association with the onset of CD in the overall Malaysian population. However, in stratification analysis, the heterozygous C/G genotype of rs10974944 was found to increase risk for CD in the Chinese population (P=0.0176; OR=2.645). For genotype-phenotype association analysis, the homozygous C genotype (P=0.0247) and allele A (P=0.0268) of rs10758669 were found to associate with inflammation at the upper GI tract in CD patients. The heterozygous C/T genotype of rs7849191 was found to reduce risk for colonic CD (P=0.038; OR=0.395) and it was also observed to be associated with the extra-intestinal complication (arthritis) (P=0.0181; OR=5.238). In conclusion, JAK2 rs10974944 polymorphism was significantly associated with CD onset in Chinese population and further study could be conducted to investigate its effect on CD.

Keywords: Crohn’s disease; Janus Kinase 2 gene; SNPs; genotyping.

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