The association between polymorphism in HLA-A, HLA-B, HLA-DR and DG genes of gastric cancer and duodenal ulcer patients with multiple EPIYA-C repeats among cagA-positive Helicobacter pylori strains: the first study in Turkish population

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Background: Polymorphisms in HLA genes are also associated with the development or prevention of gastric cancer in Helicobacter pylori-infected individuals. H. pylori strains with EPIYA-C repeats are significantly associated with gastric cancer. We aimed to evaluate the association between polymorphism in HLA-A, HLA-B, HLA-DR and DQ genes of gastric cancer and duodenal ulcer patients and multiple (≥2) EPIYA-C repeats among cagA-positive H. pylori strains for the first time in Turkey.

Materials/methods: The study and control groups were formed from 94 H. pylori strains (44, gastric cancer, 50 duodenal ulcer patients) and 86 H. pylori strains (50, non-ulcer dyspepsia patients, 36 individuals with normal gastrointestinal system), respectively. cagA and EPIYA-C pattern were determined by PCR method. DNA from peripheral blood samples was obtained by EZ-DNA extraction kit. HLA-A, -B, -C, -DRA1, DRB1, DRQA1 and DQB1 loci genotyping were performed by eRES SSO HLA Typing Kits and HLA-DQB1 loci genotyping were performed by SSO HLA Typing Kits.

Results: Multiple (≥2) EPIYA-C repeats with cagA positivity were detected in 66 (70.2%), and 2 (3.03%) of the study group and control group strains, respectively. When the two groups were compared, HLA-A 02 (OR: 1.579 95% C.I (1.021-2.442) , HLA-DQA1 01 (OR:1.848 95% C.I (1.215-2.811) ) and HLA-DQB1 06 (OR:1.821 95% C.I (1.163-2.850) alleles were detected significantly higher for the gastric cancer and duodenal ulcer risk due to the multivariate logistic regression analysis. cagA+(≥2) EPIYA-C repeats was used for the discrimination of groups. The frequencies of HLA-A 02, HLA-DQA1 01 and HLA-DQB1 06 alleles were detected as 45.2%, 40.9% and 36.9%, respectively due to the cagA+(≥2) EPIYA-C positivity. These alleles exhibited high odds ratios for HLA-A 02 [p=0.0042, OR:101.4, 95%CI 4.2-2398.4], HLA-DQA1 01 [p=0.0047, OR:69, 95%CI 3.6-1299.9] and HLA-DQB1 06 02 [p=0.0208, OR:35, 95%CI 1.71-712.9] in gastric cancer and duodenal ulcer risk in the discrimination of groups with cagA+(≥2) EPIYA-C.

Conclusions: HLA-A 02 allele exhibited the highest OR (101.4). We may suggest that individuals with HLA-A 02 allele may have 101 folds higher gastric cancer or duodenal ulcer risk than individuals with other HLA alleles when infected with H. pylori strains with cagA+(≥2) EPIYA-C repeats.