**Higher Risk of Genetic Variants of CYP1A1 with Gallstone-Independent Gallbladder Cancer Susceptibility in North India**

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**Background:** Gallbladder cancer (GBC) is one of the commonest biliary tract tumors seen in North India. However, its treatment is challenging and the prognosis is dismal. Epidemiologic studies provide evidence about individuals’ susceptibility to cancer modulation by both genetic as well as environmental factors. Xenobiotic metabolizing enzymes act as a first line of defense against environmental carcinogens and most of the cancers arise as a consequence of contact with these carcinogens. The inter-individual differences in the effectiveness of the activation/detoxification of environmental carcinogens may play a crucial role in cancer susceptibility.

**Methods:** The present study was conducted in 640 subjects including 410 GBC patients and 230 healthy subjects from North India. This study examined association of CYP1A1-MspI, CYP1A1-Ile462Val and CYP1B1 with GBC susceptibility. Genotyping was carried out by PCR-RFLP. Statistical analysis was done by SPSS ver16. Haplotype analysis was done by SNPstats.

**Results:** CYP1A1-MspI [CC] and [iso/val] CYP1A1-Ile462Val genotypes were found to be significantly associated with the carcinoma of gallbladder cancer (GBC) [*p = 0.006, p = 0.03* respectively], as compared to healthy controls while CYP1B1-Val432Leu was not associated with GBC risk. CYP1A1 haplotype [C-val] showed significant association with GBC risk [*p = 0.006*]. On stratification based on gender, CYP1A1-MspI [CC] genotype showed increased risk of GBC in females [*p = 0.018*]. In case-only analysis, tobacco users with CYP1A1-MspI [CT] genotypes were at higher risk of GBC [*p = 0.008*]. Subdividing the gallbladder carcinoma patients on the basis of gallstone status, CYP1A1 haplotype [C-val] imparted higher risk in patients without stones when compared to controls [*p = 0.018*]. The results remained significant even after applying Bonferroni correction for multiple comparisons. On applying Multivariate analysis the increased risk of CYP1A1 iso/val and val/val genotypes was observed in obese GBC patients having BMI >25 [*p = 0.021*].

**Conclusion:** The present study showed that CYP1A1-MspI, CYP1A1-Ile462Val and CYP1B1 with GBC susceptibility. Genotyping was carried out by PCR-RFLP. Statistical analysis was done by SPSS ver16. Haplotype analysis was done by SNPstats.

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