

Assessing the role of Genetic Predisposition in patients with Multiple Primary Cancers

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Upper Aero Digestive Tract (UADT) cancers are the most common cancers in India. ~8% of patients with single UADT cancer subsequently develop Multiple Primary Neoplasia (MPN) mostly within the UADT. While field cancerisation is one explanation for MPN, inter-individual differences in genetic susceptibility can be an important for risk determinant of MPN. Cumulative effect of genetic polymorphisms in low penetrance alleles, which protect the genome, may play an important role in MPN aetiology. In our case-control study we hypothesize that MPN may be a manifestation of polygenic susceptibility to carcinogens; serving as a biological model to understand gene-environment interactions.

In the present study genotyping polymorphisms of *GSTM1*, *GSTT1*, *GSTP1*, *SULT1A1* of the carcinogen metabolism, *XRCC1*, *hOGG1*, *XPB* of DNA repair and *p53* and *FAS* of the apoptosis regulation, *Cyclin D1* of cell cycle pathway was done in 160 MPN cases and 180 healthy controls by PCR-RFLP/DHPLC/ sequencing. The cases included Indian MPN patients with at least one primary in the UADT and patients with none of the primaries in the UADT, the controls were chronic tobacco habitués matched for age and gender. Difference in the genotype prevalence was calculated using Chi square test. Flow cytometry analysis of apoptotic response to tobacco specific carcinogen BPDE was done in lymphoblastoid cell lines established from patients and controls

SNPs in *hOGG1*, *SULT1A1*, *XRCC1* show marked difference in their prevalence in patients with MPN versus controls. The analysis of cumulative effect of all the candidate genes and phenotype analysis in predisposing to MPN will be presented. This study supports a multigenic pathway based approach to risk assessment in UADT cancers.

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