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Thesis title: Comparative study on endometrial and cervical cancer: with special reference to HPV-16

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Findings Key words: Human papilloma virus, uterine cervix, corpus uteri, endometrial cancer, cervical cancer, IL6, IL10, TLR9

The study subjects include 300 tissue biopsy samples of endometrium and cervix (cases and control). Genomic DNA was isolated by Proteinase K method and HPV was detected in the samples by PCR amplification followed by genotyping in cytokine encoding genes via amplification refractory mutation-specific (ARMS) PCR methodology. Further molecular landscapes of cytokine encoding genes were developed using *in-silico* approaches. Finally statistical analysis, excel 365 version and GraphPad_Prism_8.0.2.263 were used for finding the allelic frequencies and association of clinicopathological parameters with the disease. Chi-square, ANOVA, 95% CI, P value, and OR tests were performed. About 81% of Cax patients and 9% of cervix controls were positive for HPV. However only 5% of Ec patient's samples were positive for HPV and all negative in the control group. The substantial role of HPV in the advancement of Cax in both age groups (>50 years and ≤50 years) was found. However, the role of HPV was found significant in the advancement of Ec in ≤50 years age group only. For IL6 gene promoter SNPs at -174 G/C, the significant association was shown with increased risk of endometrial pre-cancer group in recessive and co-dominant model having CC genotype. For IL10 and TLR9 gene promoter SNPs, no statistical significance was found at various loci genotyped in the selected genes but for SNP -819 C/T (rs1800871), the role of 'T' allele was dominating in the development of endometrial cancer. When the serum concentration was observed, IL6 was found to be gradually increasing in cases than in control whereas the serum concentration of IL10 was observed to decrease. The stability of proteins due to the presence of deleterious nsSNPs was found mostly to decrease. The cumulative results suggested the tissue specificity of 3 deleterious nsSNPs in IL6 gene, 4 deleterious nsSNPs in IL10 gene and 2 deleterious nsSNPs in TLR9 gene to be severe for uterine corpus endometrial carcinoma. For cervical adenocarcinoma (CESC) only one deleterious nsSNPs in IL10 gene was found to be severely associated with the disease. In conclusion, this study is the first study in Indian women to perform a comparative study between cervical and endometrial cancer. The present study was successfully able to provide an updated estimate of HPV prevalence and its high-risk genotypes HPV16 and HPV18 in cervix and endometrium with or without carcinoma among Indian women. The SNPs found in the present study may serve as prospective biomarkers in the near future.

