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Epigenetic alterations of p16 gene and its prognostic role in epithelial ovarian carcinoma (EOC) patients

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Background: Novel strategies for early detection of EOC, the most common and second most lethal cancer in Indian women, are urgently needed. Silencing tumor suppressor genes via DNA methylation has established hypermethylation as one of the most frequent molecular alterations that may initiate and drive many types of human neoplasia including EOC .To determine the alterations of tumor suppressor gene p16INK4A in EOC patients to explore the possibilities of identifying potential minimally invasive markers in blood of the patients, which could help in the clinical practice as a diagnostic and prognostic marker.

Methods: Fifty EOC patients with primary epithelial ovarian cancer were selected for the study; these patients were followed for a median of 20 months. Genomic DNA extracted from fresh peripheral blood & serum followed by sodium bisulfate modification .The p16 methylation was detected using methylation-specific PCR (MSP). The p16 methylation status was correlated with age, stage, menopause, Ca125.5 and clinic pathological features.

Results: The frequency of p16 methylation in EOC patients was found to be 84%. Aberrant methylation of p16 was associated with age at diagnosis (P = 0.043). The significant association was seen with age,menopause, Patients with high methylation indices had poor prognosis (p<0.001, Hazards ratio=14.58) with age (P = 0.043), and tumor stage (P = 0.033). Aberrant methylation of p16 was strongly associated with EOC patients (P = 0.037).

Conclusions: our results that the methylated loci of TSGs (p16) may be employed as clinically useful biomarkers for prognosis and diagnosis of EOC noninvasively using readily available body fluid by MS-PCR and proved to be efficient and cost-effective method.

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