Abstract ID: - 119

Abstract Topic: - Cancer

Abstract Title: - VEGF and VEGFR2 Polymorphisms and Esophageal Cancer Risk: A Case-Control Study

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Aims: - Angiogenesis plays an important role in the growth, development and progression of solid tumors including esophageal cancer. Vascular endothelial growth factor (VEGF) and its receptors play an important role in angiogenesis. Genetic polymorphisms in VEGF and VEGFRs may affect the expression or activity of the encoded protein, ultimately influencing individual cancer susceptibility. The present study attempts to evaluate the association of VEGF +405G/C, VEGF -7C/T, VEGFR2 -604T/C and VEGFR2 1192G/A polymorphisms with esophageal cancer risk in patients from Punjab, North-West India.

Methods: - In the present study, 311 esophageal cancer patients (138 males and 173 females) and 356 healthy controls (164 males and 192 females) were investigated. VEGF +405G/C, VEGFR2 -604T/C and VEGFR2 1192G/A polymorphisms were screened using polymerase chain reaction-restriction fragment length polymorphism method, whereas VEGF -7C/T polymorphism was screened by amplification refractory mutation system-polymerase chain reaction method.

Results: - The CT genotype (OR= 0.64, 95% CI= 0.43-0.94; p= 0.02) and T allele (OR= 0.67, 95% CI= 0.48-0.93; p= 0.017) of VEGF -7C/T polymorphism were significantly associated with decreased risk of esophageal cancer. TC genotype of VEGFR2 -604T/C polymorphism was significantly associated with decreased risk of esophageal cancer (OR= 0.63, 95% CI= 0.43-0.92; p= 0.01). There was no association of VEGF +405G/C and VEGFR2 1192G/A polymorphisms with esophageal cancer risk ($p>0.05$). Genetic model analysis revealed that VEGF -7C/T polymorphism showed a decreased risk of esophageal cancer under dominant, overdominant and log-additive models ($p<0.05$). VEGFR2 -604T/C polymorphism was associated with decreased esophageal cancer risk under dominant model ($p<0.05$). Haplotype analysis revealed that GT haplotype of VEGF -405G/C and -7C/T polymorphisms was significantly associated with decreased risk of esophageal cancer (OR= 0.66, 95% CI= 0.46-0.96; p= 0.029).

Conclusions: - The present study concluded that VEGF -7C/T and VEGFR2 -604T/C polymorphisms were significantly associated with decreased risk of esophageal cancer in North-West Indians.

Keywords: - The CT genotype (OR= 0.64, 95% CI= 0.43-0.94; p= 0.02) and T allele (OR= 0.67, 95% CI= 0.48-0.93; p= 0.017) of VEGF -7C/T polymorphism were significantly associated with decreased risk of esophageal cancer. TC genotype of VEGFR2 -604T/C polymorphism was significantly associated with decreased risk of esophageal cancer (OR= 0.63, 95% CI= 0.43-0.92; p= 0.01). There was no association of VEGF +405G/C and VEGFR2 1192G/A polymorphisms with esophageal cancer risk (p>0.05). Genetic

model analysis revealed that VEGF -7C/T polymorphism showed a decreased risk of esophageal cancer under dominant, overdominant and log-additive models ($p<0.05$). VEGFR2 -604T/C polymorphism was associated with decreased esophageal cancer risk under dominant model ($p<0.05$). Haplotype analysis revealed that GT haplotype of VEGF -405G/C and -7C/T polymorphisms was significantly associated with decreased risk of esophageal cancer (OR= 0.66, 95% CI= 0.46-0.96; p= 0.029).