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Abstract Topic: - Molecular effects of genetic variation

Abstract Title: - Association of VEGF Promoter and HIF1A Exonic Polymorphisms with Infertility Risk in North-West Indians

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Aims: - Infertility is a serious clinical problem affecting couples psychologically, socially and medically. Hypoxia has a significant effect on different molecular pathways coordinating several cellular functions including proliferation, apoptosis and angiogenesis. HIF1A is the key regulator of hypoxia and modulates gene expression in several critical pathways. Vascular endothelial growth factor (VEGF) plays multifaceted roles in embryo implantation and alteration of the expression of VEGF could lead to infertility and pregnancy complications. The aim of the study was to investigate the association of three VEGF promoter (-2578C/A, -2549I/D, -460T/C) and three HIF1A exonic (g.C1772T, g.G1790A and g.C111A) polymorphisms with infertility risk in patients from Punjab, North India.

Methods: - In the present study, 193 clinically confirmed infertile patients and 213 age and gender matched healthy controls were investigated. The genomic DNA was extracted from the blood samples using the standard phenol-chloroform method. The quantity and the quality of the DNA samples were checked on 1% ethidium bromide stained agarose gel. Association of three VEGF promoter and three HIF1A exonic polymorphisms were evaluated in this study. VEGFA -2578C/A, -460T/C, HIF1Ag.C1772T, g.G1790 and g.C111A polymorphisms were genotyped using Polymerase Chain Reaction- Restriction Fragment Length Polymorphism whereas genotyping of VEGF-2549I/D polymorphism was done using the direct-PCR.

Results: - VEGF-2549II genotype and I allele, VEGF-2578AA genotype and VEGF-460CC genotype were significantly associated with increased risk to infertility. Analysis of the data under different genetic models revealed a significantly increased risk under co dominant (p=0.02), recessive (p=0.02) and log additive model (p=0.03) for VEGF-2549I/D polymorphism whereas VEGF-2578C/A polymorphism was associated with increased risk under co dominant (p=0.03) and recessive (p=0.03) genetic models.VEGF-460T/C polymorphism was associated with increased risk under co dominant (p=0.04) and recessive model (p=0.04) only. For HIF1A g.G1790A and HIF1A g.C111A polymorphisms, all the patients and controls had GG and AA genotypes respectively. There was no significant difference in the genotype frequency between patients and controls for HIF1A g.C1772T polymorphism.

Conclusions: - This study suggests that VEGF -2578C/A, -2549I/D and -460T/C polymorphisms were associated with increased risk of infertility in the patients from Punjab, North India.

Keywords: - VEGF-2549II genotype and I allele, VEGF-2578AA genotype and VEGF-460CC genotype were significantly associated with increased risk to infertility. Analysis of the data under different genetic models revealed a significantly increased risk under co dominant (p=0.02), recessive (p=0.02) and log additive model (p=0.03) for VEGF-2549I/D polymorphism whereas VEGF-2578C/A polymorphism was associated with increased risk under co dominant (p=0.03) and recessive (p=0.03) genetic models.VEGF-460T/C polymorphism was associated with increased risk under co dominant (p=0.04) and recessive model (p=0.04) only. For HIF1A g.G1790A and HIF1A g.C111A polymorphisms, all the patients and controls had GG and AA genotypes respectively. There was no significant difference in the genotype frequency between patients and controls for HIF1A g.C1772T polymorphism.