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ASSOCIATION OF FGFR4 388G/A POLYMORPHISM AS A BIOMARKER IN SUBJECTS WITH ORAL SUBMUCOUS FIBROSIS (OSMF) OF NORTH KARNATAKA POPULATION.

By

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ABSTRACT

BACKGROUND AND OBJECTIVES: Oral cancer imposes a considerable problem worldwide being a highly lethal and disfiguring disease. A single nucleotide polymorphism (SNP) in exon 9 results in an amino acid change (substitution of a glycine residue for an arginine - Gly388Arg) within FGFR4 transmembrane domain and has positive correlation with prognostic parameters in several human cancers, including breast, colon, lung, prostate, head and neck cancers and squamous cell carcinoma of mouth and oropharynx, but no studies have been done to validate the association of FGFR4 Gly388Arg with potentially premalignant conditions like Oral submucous fibrosis (OSMF). An estimate from 1996 indicated that globally, about 2.5 million people have OSMF, but studies have found that over 5 million people are affected in India alone (0.5% of the Indian population). It is also estimated that up to 20% of the world's population use betel nut in some form, so the incidence of OSMF is likely to be much higher than current estimates suggest, and it is regarded as a public health issue in India. Keeping in view the malignant transformation rate of OSMF being 7-30%, So it is extremely important to study the FGFR4 Gly388Arg association with the disease and establish it as novel biomarker by noninvasive study.

METHODOLOGY: The sample size comprised of 30 patients with Oral submucous fibrosis and 20 controls free from the lesions. A detailed history of the subjects was recorded following which clinical examination was done. Saliva sample was collected from all the subjects participating in the study. Genomic DNA extraction and PCR amplification were done.The polymorphism was detected by polymerase chain reaction-based restriction analysis.

RESULTS: In this present study males 27(90%) had a higher preponderance than females 3(10%). 76% of the study samples were in the age group of 21-40yrs suggesting that OSMF is more commonly seen in this age group. Predominantly in this study around 13.33% of the cases were below 20yrs of age. Gly/Gly genotype was seen in 70% of the cases and 85% of the controls, 13.33% of the cases and 10% of the controls show Gly/Arg polymorphism, 16.66% of the cases and 5% controls show Arg/Arg polymorphism. Even though p value >0.05 in the present study each findings are considered statistically significant, considering 10% level of significance. The frequency of the ''Arg'' allele in the patient group (23.3%) was greater than that in the control group (10%). 23.3% of OSMF cases showing Arg allele in the current sample is again a statistically significant finding. However, there was no significant correlation between the association of habits, frequency of habits, duration of quid placement and site of quid placement with the nature of polymorphism.

CONCLUSION: Further research is required to understand the possible role of FGFR4 Gly388Arg in malignant transformation of OSMF. The studies in this aspect could be designed with a larger sample size and also other associated habits like smoking and alcohol can be considered. However in this present study we conclude that FGFR4 Gly388Arg has the potential application as prognostic marker in predicting the outcome of the disease.

KEY WORDS: Oral cancer, FGFR4, Oral submucous fibrosis, Polymorphism