A Short Review on Human Leukocyte Antigens and Oral Submucous Fibrosis
Vijaykumar Goudappagouda Biradar, Madhusudan Astekar

Abstract
Human leukocyte antigens are crucial components of host defense against microbial challenge but the associations of Human leukocyte antigens types with oral diseases have not been studied in detail. Oral submucous fibrosis is a complex, debilitating, and precancerous condition. Formerly confined to the Indian subcontinent, it is now often seen in the Asian populations of the United Kingdom, USA and other developed countries, and is therefore a serious problem for global health. Human leukocyte antigens typing reveals the genetic and molecular changes related to early, intermediate and late endpoints in the process of oral carcinogenesis. There are only few studies on the Human leukocyte antigens typing of oral submucous fibrosis in the worldwide in recent years. This article attempts to compile details of Human leukocyte antigens typing in Oral submucous fibrosis and summarize and infer on the findings.

Keywords: Genetic Risk; Human Leukocyte Antigens; Molecular Changes; Major Histocompatibility Complex; Oral Submucous Fibrosis; Precancerous Condition

Introduction
Oral submucous fibrosis (OSF) is a premalignant condition that primarily affects the oral cavity. The clinical hallmark of this disease is the development of progressive trismus. The latter is a direct consequence of loss of the normal fibro-elasticity of the oral mucosa and replacement of the fibro muscular connective tissue by the deposition of dense collagen. Oral submucous fibrosis is a prototype of pathological fibrosis sharing characteristics in common with other organ involvements where deposition of collagen is taking place primarily in the oral submucosa.

The etiopathogenesis of oral submucous fibrosis believed to be multifactorial includes areca-nut chewing, ingestion of chilies, genetic and immunologic processes, nutritional deficiencies and other factors. The pathogenesis of oral submucous fibrosis and the pathways that leads to progressive fibrosis, culminating in extreme difficulty of mouth functions have always aroused curiosity but still remains enigmatic. What need to be elucidated are mainly molecular pathways and also those that lead to its ultimate malignant transformation. Different hypothesis have been put forward in fully elucidating the pathogenic sequence of this disease.

Major histocompatibility complex (MHC) classes I and II molecules, called human leukocyte antigens (HLA), have a pivotal role in immune response. Pathogen-derived antigens are recognized by T-cells in the form of peptides that are bound to human leukocyte antigens molecules after antigen processing. Human leukocyte antigens molecules vary extensively between individuals which may explain differences in inflammatory response towards microbial challenge. However, the associations of human leukocyte antigens class I (HLA-A, -B and -C) and II antigens (HLA-DR, -DQ and -DP) with oral diseases have not been studied extensively. Particularly, studies on possible HLA associations among generally healthy subjects are scarce.

There is substantial evidence to support oral submucous fibrosis as an inheritable disease. A number of genetic polymorphisms have been associated with risk for oral submucous fibrosis in various populations. Since host susceptibility may be defined in terms of genetic makeup of the individual, a relatively recent focus in Oral submucous fibrosis has been to quantify genetic risk and identify specific role that genes play in determining host susceptibility. At present, the specific role that genes play in defining susceptibility remains largely unidentified. The main objective of this review knows the role of Human leukocyte antigens in association with Oral submucous fibrosis.
Discussion
Human Leukocyte Antigens or the Major Histocompatibility Complex has been considered as candidate marker for oral submucous fibrosis because they are involved in regulating immune responses. 6, 11 HLA system is the name of the major histocompatibility complex in humans. The super locus contains a large number of genes related to the immune system function in humans. This group of genes resides on chromosome 6 and encodes cell-surface antigen-presenting proteins and many other genes. The major HLA antigens are essential elements for immune function. They are important in disease defense and organ transplant rejections. They may protect against or fail to protect (if down regulated by an infection) against cancers and may mediate autoimmune disease (e.g. Type I diabetes, coeliac disease). 11

Impairment of the immune system has long been propagated as a mechanism in the pathogenesis of OSF. The geographical location and the almost definite association with habit of chewing betel nut have led to suggestions of an autoimmune basis for the condition. Assessment of HLA antibodies in patients with OSF lends some credence to this suggestion. In one of the earliest studies on HLA prototypes, Canniff et al., 12 evaluated HLA type A10 and DR3 in OSF patients. The authors found conclusive evidence of raised expression of these prototypes in OSF patients. They opine “the results support the concept that OSF is a chronic autoimmune disease, initiated by constituents of betel nut, and occurring in genetically susceptible individuals.” It was also suggested by them that genes situated in the HLA region are important determinants of genetic susceptibility in OSF. In contrast, in studies on larger samples of betel nut chewers in South African subjects of Indian origin, Van Wyk et al., 13 could not find any significant association of HLA antigens and have discarded the hypothesis of autoimmunity for this disorder.

The variations and discrepancies in the results of these studies could be because of differences in the characteristics in the group studies, OSF diagnostic methods used and the HLA typing methods used. The characteristics of the groups included sample size, race, age, sex and socioeconomic status of the study and control subjects. In our opinion although these variations and discrepancies of characteristics, diagnostic methods and HLA typing methods used could play areole, but the major part is taken by the difference in the strong ethnic component which predisposes certain population to risk of OSF. Studies like this which are related to individual gene would help by contributing to the existing scientific knowledge and providing a better understanding of this condition. This will help not only the individual at risk but also help to formulate intervention strategies towards better management of these individuals.

Conclusion
Oral submucous fibrosis is a potent precancerous condition of oral mucosa, assuming epidemic proportions in Indian subcontinent. The etiology of this condition is assumed to be multifactorial. The nature of this disease remains enigmatic and pathogenesis is obscure. However, this review was valuable in terms of identifying opportunities to provide recommendations for future research, in terms of the populations to research, the types of interventions needed, the types of outcomes to be measured, the study designs needed, and the infrastructure required to conduct studies.

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Author Affiliation
1. Dr. Vijaykumar Goudappagouda Biradar, Ph.D., Scholar, Reader, Jaipur Dental College, Jaipur, Rajasthan, 2. Dr. Madhusudan Astekar, Professor and Head, Department of Oral Pathology, Institute of Dental Sciences, Bareilly-243006, UP, India.

References

Corresponding Author
Dr.Vijaykumar Biradar,
Reader, Dept. of Oral Pathology,
Jaipur Dental College, Jaipur,
Rajasthan State, India.
Ph: 09694610945
E-mail: drvijay06_biradar@yahoo.com

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