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RESEARCH ARTICLE

EVALUATION OF ABO BLOOD GROUP SYSTEM IN PATIENTS SUFFERING FROM ORAL SUB
MUCOUS FIBROSIS

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ABSTRACT

Oral submucous fibrosis (OSF) is a potentially malignant disorder of oral mucosa associated with multifactorial etiology such as areca nut chewing, nutritional deficiencies, ingestion of chillies, genetic susceptibility and immunologic predisposition. This condition is well recognised for its malignant potential and is particularly associated with areca nut and tobacco chewing, which is a habit practiced predominately in Southeast Asia and India with the overall prevalence rate of about 0.2% to 0.5 %. Since blood group antigens are also found in epithelial cells of oral mucosa, various studies have shown the relationship of ABO blood group with certain diseases. Based on this background the aim of the present study was to evaluate the relationship of ABO blood grouping system in patients suffering from OSF.

Materials and methods: The present study was undertaken at the Department Of Oral Pathology, Microbiology And Forensic Odontology, School of Dental Sciences; KIMSDU, Karad after obtaining the permission from the ethical committee of the Institution. The study sample comprised of 50 cases of Oral sub mucous fibrosis and 50 controls and statistical analysis were assessed to evaluate the relationship of ABO blood group and OSF.

Results: The result for the study revealed that people with blood group B were at higher risk of developing OSF as compared to other groups.

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INTRODUCTION

Oral Submucous fibrosis (OSF) is a potentially malignant disorder of oral cavity. (Rasika Priyadharshani *et al.*, 2013) It is a chronic, progressive disease which was first described by Schwartz in 1952. (Angadi and Rekha, 2011) In 1966, Pindborg defined OSF as, "an insidious, chronic disease affecting any part of oral cavity and sometimes pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxtaepithelial inflammatory reaction followed by a fibroelastic change of lamina propria, with epithelial atrophy leading to stiffness of oral mucosa and causing trismus and inability to eat".

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(Pindborg and Sirsat, 1994; Rajendran, 1994) The precancerous condition of OSF, first postulated by Paymaster, (Rajendran, 1994) is well recognised for its malignant potential of 7-13% to oral carcinoma and is particularly associated with areca nut and tobacco chewing, which is a habit practiced predominately in Southeast Asia and India with the overall prevalence rate of about 0.2% to 0.5 %. (Rasika Priyadharshani *et al.*, 2013; Vanaja Reddy *et al.*, 2011) ABO blood grouping system with its antigens is major alloantigens and a stable feature of human population. Since ABO antigens are confined not only to the RBC membrane but also found in epithelial cells of the oral mucosa and undergo profound changes in expression during cellular differentiation and malignant development, several studies have been conducted in the past decades on possible relationship of ABO blood group to certain diseases. The first association between the ABO blood group

and cancer risk was reported in 1953 in English patients with stomach cancer, where blood group A was associated with increased risk of stomach cancer. (Seth Rummell *et al.*, 2012) Similarly studies conducted by Tyagi *et al.* 1965; Mittal *et al.* (1969) and Bushranaaz *et al.* (Bushranaaz and Ramesh, 2012) have shown that individuals with blood group A have a predisposition for oral cancer.

OSF now being classified as potentially malignant disorder of oral mucosa with the prevalence rate of 0.2% to 0.5 %. In Southeast Asia and India. It is well recognised for its malignant potential rate of 7-13%. (Rasika Priyadharshani *et al.*, 2013) "Recently" it has been proposed that oral cancers arising in OSF constitute a clinicopathologically distinct disease. One study recognized that most of these patients are younger males with better prognostic factors, whereas another retrospective study in China reported contradictory data stating that OSCC originated from OSF is clinically more invasive and also exhibits higher metastasis and recurrence rate than OSCC not originated from OSF (Rasika Priyadharshani *et al.*, 2013; Vanaja Reddy *et al.*, 2011). In addition, various surveys conducted in cancer hospitals in India revealed a 15-20% frequency of oral cancer among OSF cases. (Angadi and Rekha, 2011) This finding of a high frequency of OSF among oral cancer patients in India (e.g., 40 among 100 oral cancer patients) alerts the clinician for its early diagnosis and treatment. Based on this background, the present study was undertaken within the field of research to assess the relationship between ABO blood group and OSMF patients that in turn will lead to early diagnosis of oral squamous-cell carcinoma (OSCC) arising in the background of OSF.

MATERIALS AND METHODS

The present study was undertaken at the Department Of Oral Pathology, Microbiology And Forensic Odontology, School Of Dental Sciences; KIMSUDU, Karad, after due approval of the ethical committee. A total of 100 cases – 50 clinically diagnosed cases of OSMF as per the criteria described by Bailoor (1993) as grade I, grade II and grade III and 50 control group were considered in the study. Clinical details included name, age, gender and different tissue abuse habits like chewing panmasala with or without tobacco, gutkha chewing, areca nut chewing, plain tobacco, mawa, smoking, alcohol. Moreover duration of habit in years, frequency of habit per day, style of chewing i.e. spitting, swallowing and also duration taken to chew was recorded. Blood samples of both the case group and control group were collected, which were investigated for their blood groups. Blood groups on the subjects were analyzed by placing a drop of blood on the slide and treated with anti-A and anti-B sera.

Positive agglutination of the blood on treating with anti-A is considered as blood group A, positive reaction with anti-B is considered as blood group B, if no agglutination is produced, then the blood group is O and if agglutination is seen with both anti-sera, then blood group AB is considered. Similarly, positive agglutination reaction with Rh antigen is considered Rh positive or otherwise as Rh negative. The data collected was subjected to statistical analysis, and the results obtained are as shown in Table 1 & 2.

RESULTS

Majority of the subjects in the study belonged to blood group B. Out of 50 clinically detected cases of OSF, blood group B was most prevalent with 48% whereas A, O and AB blood groups with 18%, 24% and 10% respectively. P value for A, B, AB, O blood groups is 0.354. Table 1 and 2 shows the distribution of ABO blood groups and Odd's ratio among case and control groups.

Table 1. Blood group characteristics in case and control group

SUBJECTS	CASE GROUP	CONTROL GROUP
Blood group A	18%	22%
Blood group B	48%	36%
Blood group AB	10%	18%
Blood group O	24%	24%

Table 2. Odds ratio showing the association of ABO blood group and OSF

BLOOD GROUP	ODDS RATIO
A	1.34(1.05-1.40)
B	1.56(1.20-0.55)
AB	0.45(0.25-0.75)
O	0.85(0.45-0.35)

DISCUSSION

Oral submucous fibrosis is a potentially malignant disorder predominantly seen in people of Southeast Asia and India. The reason for the rapid increase as the disease in this geographic area is reported to be due to an upsurge in the popularity of commercially prepared arecanut preparations in Southeast Asia and India. The main aetiological agent causing the disease is confirmed as arecoline in arecanut which contains definite carcinogens, thus promoting oral carcinogenesis. Multifactorial etiology that includes genetic susceptibility, nutritional deficiency and ingestion of spicy foods is also considered to be a part in the enigmatic pathogenetic mechanism for OSF. (Canniff *et al.*, 1986; Sinor *et al.*, 1990; Sirsat and Khanolkar, 1962). Human genetics has emerged as a basic biological science in understanding the health and disease. The complex interactions of endogenous factors in health and disease can be effectively studied using human genetics. Various studies in the past decades have been conducted that revealed a strong association of ABO blood groups with different oral and systemic diseases. H antigen is a blood group antigen present in all individuals irrespective of blood group types. It is the precursor for formation of A and B antigens. (Tyagi *et al.* 1965; Auclair, 1984) A wide spectrum of genetic studies such as Cytochrome P 450, single nucleotide polymorphism of TGF β 1 have provided significant evidence to support the theory of possible genetic predisposition to OSF. (Rasika Priyadharshani *et al.*, 2013) Le Pendu *et al.* (2001) also found that, the immunological reactivity of H antigen is markedly reduced in certain diseases due to changes in cell surface. (Jovanvic-cupic *et al.*, 2008) Changes in cell surface can be anticipated in OSF due to interaction of keratinocytes and fibroblasts, which is important not only in pathogenesis but also in malignant transformation as it is the proved fact that OSF is an epithelial driven connective tissue disease. ROS-related DNA damage appeared to play a important role in both pathogenesis and malignant transformation (Rasika

Priyadharshani *et al.*, 2013). Also as OSF is now classified as oral potentially malignant disorder as per the current Working Group of WHO (2005) and defined OPMD as “ a group of disorders of varying etiologies, usually tobacco; characterized by mutagen-associated, spontaneous or hereditary alterations or mutations in the genetic material of oral epithelial cells with or without clinical and histomorphological alterations that may lead to oral squamous cell carcinoma transformation.”(Oral potentially malignant disorders, 2014) Hence based on this background, the present study was conducted to assess the relationship between ABO blood grouping and OSF and to determine which blood group is more susceptible to develop OSF which in turn would lead to early diagnosis of OSCC arising in the background of OSF.

The present study demonstrated that there exists a relationship between ABO blood groups and OSF. People having blood group B were found to have a greater tendency to develop OSF. This can be explained by the fact that blood group antigens, in addition to being present on red cell membranes is also found on oral epithelial cells and arecoline being the principal causative factor has an impact on keratinocytes causing cell cycle dysregulation, hypoxia, processes leading to DNA double strand breaks, senescence and many other pathways related to carcinogenesis. (Rasika Priyadharshani *et al.*, 2013) In this study, among the OSF cases, the male: female ratio was around 1: 2. This may be probably due to the differences in the clinical criteria for diagnosis and also the preponderance to iron and Vit B12 deficiency among the Indian females. (Angadi and Rekha, 2011) also the highest frequency of OSF cases irrespective of blood groups was seen in the age group of 20-45 years which was in accordance with the well documented fact that OSF cases occur mostly at an early age. Arecanut chewing is the main etiological factor in OSF. The same was reflected in the study wherein the frequency of OSF was highest among those who had the habit of arecanut chewing. Also in the present study it was seen that though cases of all blood groups had the habit of arecanut chewing, OSF was more seen in patients with blood group B. This can be explained by the fact that the RBC cell membrane is made up of glycoconjugates that includes carbohydrates such as ABO antigens that contain key receptor molecules like EGF receptors, integrins, cadherins and CD 44 that control cell proliferation and motility. As the expression of these receptors vary due to any carcinogenic agents like arecoline, the ABO antigens also vary resulting in various pathologies such as oral cancer, premalignant diseases, etc. (Hamed *et al.*, 2014) In the present study, there was no correlation found between Rh factor and OSF. This was in accordance to Shima *et al.* who showed no co-relation of Rh factor with oral cancer patients in a defined group of Iranian population. (Hamed *et al.*, 2014) This may be attributed to the physiological role of complex proteins of Rh factor in transportation of toxic chemicals to detoxifying organs like liver and kidney thus causing linkage disequilibrium. In 2007, Campi *et al.* (2007) showed that altered glycosylation plays a pivot role in most aspects of malignant phenotype that includes signal transduction and apoptosis. Gao *et al.* (2004) (Gao *et al.*, 2004) also demonstrated that there is significant correlation between specific ABO allelic loss and loss of A/ B antigen expression in potentially malignant lesions. Our study is first of its kind to observe the co-relation between the OSF and ABO blood group

system. Future studies with larger sample need to be carried out to confirm the role of ABO blood grouping as a neglected biomarker in various diseases and different stages of OSF.

Conclusion

By employing a simple technique of blood grouping during community field programmes, we can target people with blood group B and educate them that they are at more risk of developing OSF at early age with tobacco chewing habits. Also further research on ABO blood group as a potential biomarker for premalignant and malignant diseases should be ascertained.

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