

*Original Research***A cross sectional study based on Assessment of Association between ABO blood group and Oral Sub Mucous Fibrosis**

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Abstract: Aim: The purpose of this study is to assess any association between ABO blood groups and Oral sub mucous fibrosis. **Materials and methods:** A total of 100 cases – 50 clinically diagnosed cases of OSMF and 50 control groups (with habits of use of areca nut/tobacco in smoking/smokeless form and with no oral premalignant lesions) were considered in the study. Blood samples of both the case group and control group were collected, which were investigated for their blood groups. The data collected was subjected to statistical analysis using Chi-square test and odd ratio. P value <0.05 was considered statistically significant. **Results:** 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 and was statistically significant $p < 0.05$. **Conclusion:** This study reports that ABO blood group is significantly associated with OSMF. The subjects with blood group B have 1.32 times higher risk of developing OSMF compared to other blood groups.

Keywords: Blood group; Keratinocytes; Oral; Premalignant lesions; Submucous fibrosis.

INTRODUCTION

OSMF was first described by Sushrutha (2500–3000 BC) as Vidhari, who had recognized it as a mouth and throat melody.¹ In 1966, Pindborg defined OSMF as an “Insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded and/or associated with vesicle formation, it is always associated with juxta epithelial inflammatory reaction, followed by fibro elastic change of lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa causing trismus and inability to eat”.²

The global scenario reveals that it is predominantly reported in people of South Asian region or South Asian immigrants to other parts of the world as a result of the traditional use of Areca nut and its various preparations endemic to these areas.³ Currently, 5 million people are suffering from this precancerous condition in Indian subcontinent.⁴ The estimated prevalence of OSMF in India is in the range of 0.03–3.2%.⁵ The rate of malignant transformation of this premalignant condition is anywhere between 7–14%.⁶ The precancerous nature of OSMF was first reported by paymaster who found occurrence of OSCC in one third of his patients.⁷

The existence of blood groups in humans dates back to 20th century when Karl

Landsteiner in 1901 described the existence of serologic differences between individuals, segregating people into one of the four groups depending upon whether their red cells contained agglutininogen “A,” agglutininogen “B,” neither A nor B (O) or both A and B (AB).⁸ This invention later led to a number of serological, immunological, and genetical studies to investigate and to establish the relative susceptibility of some blood group phenotypes to certain diseases. The possibilities of the association between ABO blood group and malignancies were explored for the first time by Alexander in 1921.⁹

It was also reported that there is an existence of association between blood group antigens particularly in blood group A and oral pathologies.¹⁰ Jaleel et al., in 2012 reported that people with blood group A had 1.46 times higher risk of developing oral cancer in comparison to other groups.^{8,9} Mortazavi et al., in 2014 reported that patients with blood group B were 3.5 times at risk of developing oral cancer than others.¹¹ Akhtar et al., in 2011 reported a high incidence of oral cancers in blood group B.¹² Thus, opening new arenas in oral disease research.

In India and in western countries, many workers have tried to find out the relationship, between ABO blood groups and different forms of cancers involving various parts of the body like cervix,

stomach, breast etc. However, if such a relationship between the blood group and diseases can be established, it may be conceded that the presence of the particular blood group or genes or antigen has somehow increased the susceptibility to the diseases.¹³

Till date, there are a plethora of studies reporting the association between blood group antigens and various diseases. Limited number of studies has been reported relating blood group phenotypes with the OSMF. Hence, the present research was undertaken to evaluate whether ABO blood group is related to OSMF risk. If any such association exists, individuals who are known areca nut chewers and with susceptible blood group antigen will be counseled to quit the habit, thereby intervening the exposure to the disease at the earliest and avoiding complications.

MATERIALS AND METHODS

The present cross sectional study was undertaken at the Department Of Oral Medicine and Radiology, Rama Dental College Hospital and Research Center, Kanpur. 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 which consisted of patients with habit of using smokeless/smoking form of tobacco and areca nut and with no oral premalignant lesions were considered in the study. The age group ranged from 25-60years and the 67 males and 33 females constituted the study group.

The inclusion criteria for this study consisted of patients within the age range of 25-60years and with clinically diagnosed oral submucous fibrosis, and also the patients with (cases) and without (controls) OSMF and who were willing to give their blood samples constituted the study group. All those patients who were not willing to give their blood samples, patients with other oral premalignant lesions with /without OSMF, and patient with malignancy were excluded from the study group. 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 from the antecubital of both the case group and control group were collected, which were investigated for their blood groups. Blood groups on the subjects were analyzed based on the slide method; 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. The data collected was subjected to statistical analysis using Chi-square test and odd ratio. P value <0.05 was considered statistically significant and the results obtained are as shown in Table 1 & 2.

RESULTS

The distribution of the ABO blood groups among the cases and controls as observed in table 1 is, out of 50 clinically detected cases of OSF, blood group B was most prevalent with 52% whereas A, O and AB blood groups were 21%, 13% and 14% respectively. The p value for A, B, AB, O blood groups is <0.05 and is statistically significant (Table 1).

Table1: Blood group characteristics in case and control group.

Subjects with Blood groups	Cases N (%)	Control N (%)	p-value
A	11(21%)	13(26%)	<0.05
B	26(52%)	18(35%)	
AB	06(13%)	09(19%)	
O	07(14%)	10(20%)	
Total	50(100%)	50(100%)	

The Odd's ratio among case and control groups with the blood group B being 1.32 times at risk with the range (95% confidence interval) varying from 1.02-1.42 followed by blood groups A with the odd ration of 1.19

and the range from 1.06-1.31, O with the odd ratio of 1.03 and the range from 0.78-0.91 and AB with odd ratio of 0.87 and the range varying from 0.41-0.52. The p value for the odd ratios for the ABO blood grouping and its relation with OSMF was found to be statistically significant (<0.05). This indicates the risk of developing OSMF in patient with B blood group.

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

Blood group	Odds ratio	95% CI		p-value
		Lower	Upper	
A	1.19	1.06	1.31	<0.05
B	1.32	1.02	1.42	
AB	0.87	0.41	0.52	
O	1.03	0.78	0.91	

*CI- Confidence interval

DISCUSSION

The idea of exploring the association between human genetic make-up and disease pathology is challenging. Understanding the relationship between human genetics and disease is the current field of the interest for the researchers.¹⁴ The attempts to establish a scientific association between ABO blood group systems and various diseases dates back to 20th century following the discovery of ABO blood group antigens by Karl Landsteiner. The ABO blood group is genetically determined and therefore is not a modifiable risk factor as are cigarette smoking, body mass index, diet, or other lifestyle related variables.¹⁵

The first association between the ABO blood group and disease risk was reported in English patients with stomach cancer where blood group A was associated with increased risk of stomach cancer. It was a study report of 1930s which revealed that blood group A was associated with oral pathologies that opened new insights into oral disease research. Maxillofacial deformities were least in blood group A individuals and greater with blood group B indicating the role of ABO blood groups in various oral pathologies.¹⁰ 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 etiological 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.^{16,17}

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 histo-morphological 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.¹⁸

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.¹⁹

Our finding is in contrary with a study report of Vaish et al., in 1979 who found that blood group A is highly susceptible to OSMF and oral lichen planus (OLP), followed by O, AB, and B in logical sequence in their proportion in descending order.²⁰ It is well known that OSMF is a premalignant

condition and has the potential to transform itself into oral cancers whose genetic association with blood group antigens is well established. A study report of Tyagi et al., in 1965 revealed a non significant association of various blood groups in patients with oral cancer. However, preponderance of blood groups A and AB was observed in their study population.²¹ Another study by Mittal VP found increased incidence of oral cancer in blood group A followed by O.²² A study report of Jaleel et al., revealed that blood group A is at a greater risk to develop oral cancer in comparison to other blood groups.⁹

Our findings are in consistent with a study by Ghooi et al., found preponderance of blood group B in oral cancer patients.²³ The result of our study are also closely similar with the outcome of the study conducted by Nikam et al who also reported highest incidence of blood group B (48%) followed by O (24%), A (18%) and AB (10%). Our results in context to the odd ratio were also similar to that reported in the study conducted by Nikam et al where the odd ration value for blood group B were 1.56(1.20-0.55), A were 1.34(1.05-1.40), O were 0.85(0.45-0.35) and for blood group AB were 0.45(0.25-0.75) and the odd ratios in the present study were as follows: for blood group B 1.32(1.42-1.02), blood group A 1.19(1.31-1.06), O were 1.03(0.91-0.78) and for blood group AB were 0.87(0.52-0.41).²⁴

On the basis of present study, the statement of Bakare et al., proves to be true who said that the variants of ABO blood group might play an important role in immunology and in disease prevention.²⁵ 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 glycol conjugates 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.²⁶

Our study is one of the few studies reported in literature 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: This study reports that ABO blood group is significantly associated with OSMF. The subjects with blood group B have 1.32 times higher risk of developing OSMF compared to other blood groups. Blood groups are easily accessible factor (s) of human genetic makeup. Just by simple blood group determination, the individuals with blood group B can be identified and can be counseled to quit the habit, thereby avoiding potential complications.

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