Mapping the ABO Blood Group Landscape :Insights into Oral Cancer and Precancerous Lesions

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KEYWORDS

ABO Blood group, Oral potentially malignant disorders, Oral Cancers, Oncogenic risk, Early detection.

ABSTRACT

Introduction: Substantial literatures have revealed a connection between ABO blood group and cancer and our study seeks to explore the clinical significance of ABO blood groups in providing insight into the prevention and early detection of Oral Potentially Malignant Disorders (OPMDs) and Oral Cancer.
Materials & Methods: This study was conducted with 140 study participants. These cases were equally divided into 4 groups comprising of control, OSMF, Leukoplakia and Oral cancer respectively. Detailed history regarding tobacco and areca nut consumption was obtained and recorded. The ABO blood group determination was done using Rapid Slide Method. Results obtained were statistically analysed using Pearson's chi-square test and significant results (P value <0.05) were further processed for logistic regression (odds ratio) analysis.
Results: Through meticulous analysis, we established a noteworthy correlation between blood group 'B' and heightened susceptibility (71.43%) to the development of oral cancer.
Conclusion: Individuals with blood group 'B' were at 6.25 times higher risk of developing oral cancer as compared with other blood groups thus emphasizing the importance of such readily accessible mass screening methods.

INTRODUCTION

Indulging in the bite of tobacco, the puff of Bidi, or the swirl of cigarette smoke isn't just a habit but it's a pathway to peril. In India, where tradition meets modernity, the allure of guthkha and the lure of Zarda hold sway over too many. But behind these cultural staples lie the shadows of pre-cancerous lesions, lurking to transform into the harrowing tale of oral cancer.

Oral cancer often develops clinically as a two-stage process, the first step being the appearance of OPMD and the second step is the development of carcinoma. [1]

OPMDs like leukoplakia and OSMF shows a high prevalence with risk of malignant transformation ranging from 0.6% to 4.2%. [2]

India accounts for 40% cases of oral cancer in South Asian countries and one third of all deaths due to cancer. [3] Due to its morbidity and mortality, oral cancer has the lowest five year survival rate of less than 50%, thus, diagnosing them early would reduce the morbidity as well as mortality rates.

As we all know human genetics transcends the narrow scope of studying solely hereditary diseases. It has evolved into a fundamental biological discipline that delves into the intricacies

of both health and disease, exploring the interplay between inherent factors and environmental influences. The investigation into the association between ABO blood groups and the susceptibility to OPMDs and cancer unveils a fascinating intersection of genetics and disease pathology. The potential influence of ABO antigen in carcinogenesis has been explored by Alexander in 1921. [4]

An increasing understanding of the role played by blood group antigens in various physiological processes represents a crucial stride towards unravelling personalized risk factors in oncology. Hence, present research explored the potential correlation between ABO blood groups and OPMDs & Oral cancer triggered by Tobacco and Areca nut usage. Additionally, the study proposes an insight for risk assessment and counselling that may contribute to public health initiatives aimed to combat the huge burden of this sinister disease.

MATERIAL AND METHODS:

This cross-sectional study was conducted in duration of 2 years (April 2022- March 2024) on patients randomly selected from OPD at our hospital. Ethical clearance was obtained from the ethical committee of Vyas Dental College and Hospital, Jodhpur (Approval number – VDCH/IEC/2022/02).

Patients between age group of 21-70 years both male and female with tobacco or areca nut habits and clinically diagnosed leukoplakia or OSMF while histopathologically confirmed Oral Cancer were included. Patients with any systemic disease / medication, ex. tobacco and areca nut consumers, carcinoma on any site other than oral cavity or metastasis and patients with known blood dyscrasias were excluded. Inform consents were taken from participants.

The study samples consist of 140 subjects who were equally divided into 4 groups as below:-

Group A: Participants without any habit and lesions (**Control group**). (n=35)

Group B: Areca nut chewers with clinically confirmed **OSMF**. (n=35)

Group C: Tobacco consumers with clinically confirmed **Leukoplakia**. (n=35)

Group D: Tobacco and/or Areca nut consumers with histopathologically confirmed **Oral cancer**. (n=35)

Material Required:

1. Set of Diagnostic Tools.
2. ABO blood group testing Kit
3. Sprit, Cotton and Gauge
4. Lancet
5. Biopsy Kit

Method of Sample Collection:

The blood group determination was done using **Rapid Slide Method** (J. MITRA Combined ABD Monoclonal Antibodies for blood typing). A clean glass slides was taken and one drop anti-A, anti-B and anti-D monoclonal antibodies were placed on a slide on their respective segments. Blood sample was obtained from "finger-stick" method and one drop of whole blood sample was added to each antibody segment. Blood cells and antibodies were mixed and spread over an area of 2cm using a clean mixing stick. Slide is rocked gently from side to side and the agglutination is observed within one minute.

Agglutination of the Red Blood Cells (RBCs) with the antibodies is a positive test indicating the presence of 'A' and/or 'B' antigens on the cells and no agglutination indicates the absence of 'A' and/or 'B' antigens on the cells. Same principle of agglutination of RBCs with the antibodies is applicable for Rh factors.

Data was subjected to statistical analysis performed using SPSS version 21.0. Frequencies, percentages, mean, standard deviation, minimum and maximum values of variables were

calculated. As data was categorical; therefore, **Pearson's chi-square test** was applied for analysis. After the significant results in the overall comparison, the chi-square test with **Bonferroni correction** was applied. Whenever the expected frequency in any cell was less than 5, the chi-square test with **Yates' correction** was applied. The significant results in the chi-square test were further processed for **logistic regression (odds ratio) analysis.** P value **<0.05** was considered statistically significant.

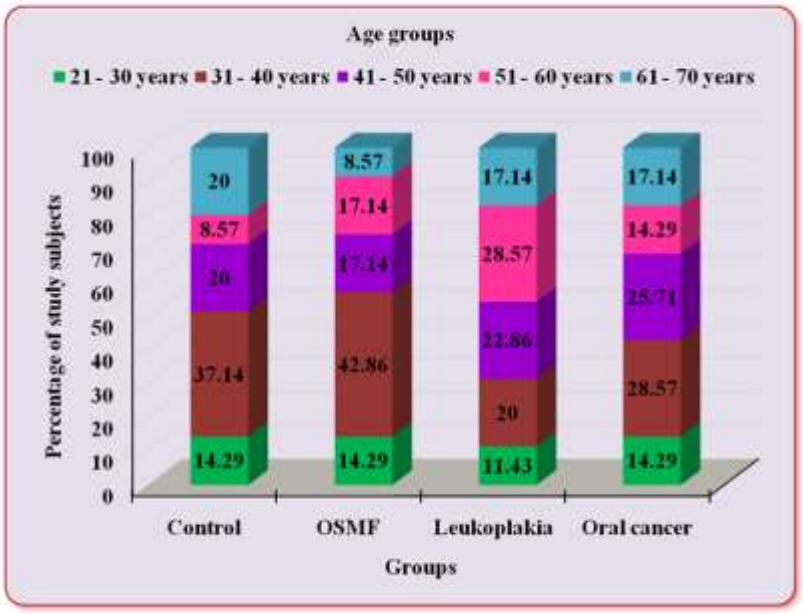
RESULTS

Chi-square test showed no significant difference between the groups for age-wise distribution (Yates' $\chi^2 = 6.773$, df = 12, P >0.05, not significant) and gender-wise distribution ($\chi^2 = 2.652$, df = 3, P >0.05, not significant) as shown in Graph -1 and 2 respectively. Graph 3 depicts the distribution of use of different tobacco products in study groups. Here, the total numbers and percentages are more than 35 in a group as some individuals were consuming more than one product. Chi-square test showed significant difference between the groups for use of different forms of tobacco (Yates' $\chi^2 = 11.118$, df = 4, P <0.05, significant).

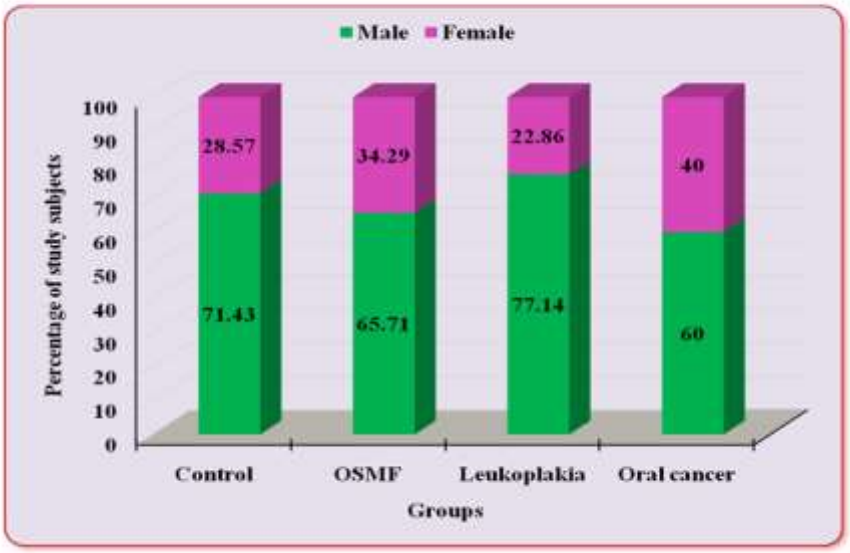
Further, the comparison among ABO blood groups and study group revealed a significant difference ($\chi^2 = 17.295$, df = 9, P <0.05, significant). In control group, 25.71%, 28.57%, 20.00%, and 25.71% participants were having blood group A, B, AB and O respectively. In OSMF group, 28.57%, 40.00%, 14.29% and 17.14% cases were having blood group A, B, AB and O respectively. In leukoplakia group, 25.71%, 34.29%, 17.14% and 22.86% had blood group A, B, AB and O respectively. In oral cancer group, 17.14%, 71.43%,5.71% and 5.71% had blood group A, B, AB and O respectively.

After the overall analysis, pairwise comparison was made according to Bonferroni correction rule, and it was inferred that numbers of cases with blood group B were significantly higher in oral cancer group than control group. ($\chi^2 = 12.857$, df = 1, P <0.002, significant).

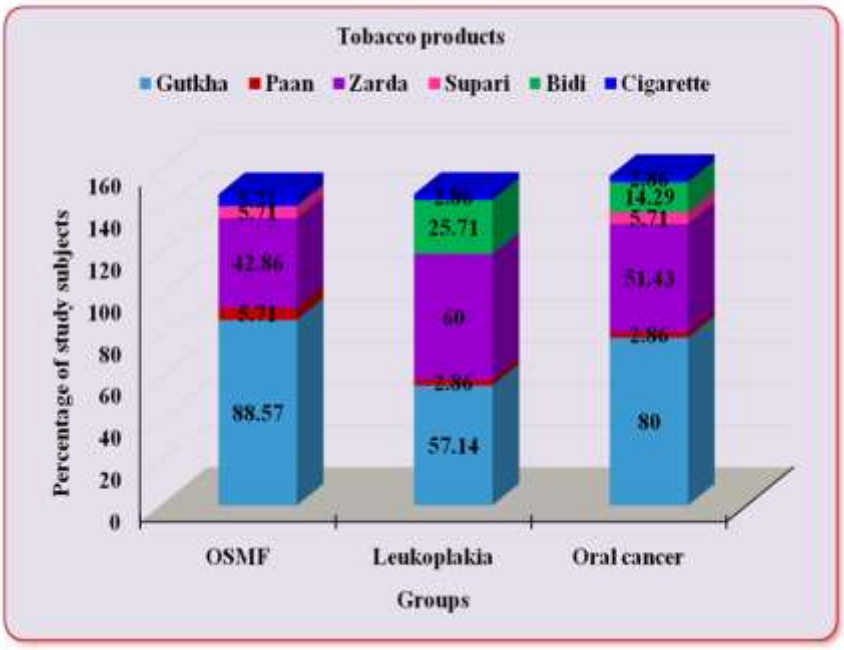
Graph 1: Age-wise distribution between Control & study groups



Graph 2: Gender-wise distribution between control & study groups



Graph 3: Distribution of use of different tobacco products in study groups



Graph 4: Frequency of ABO blood groups between control & study groups.

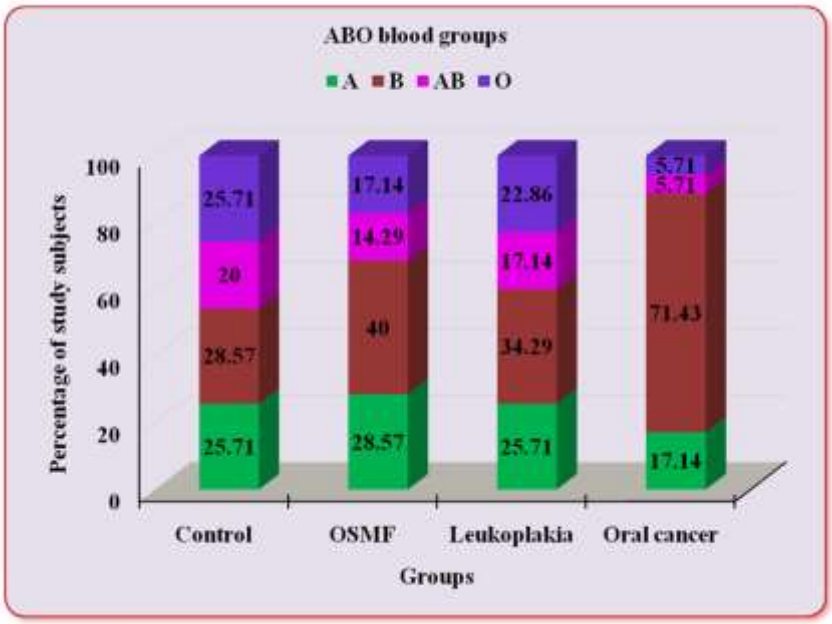


Table 1: Frequency of ABO blood groups between control & study groups.

ABO blood groups	Groups				Total
	Control	OSMF	Leukoplakia	Oral cancer	
A n (%)	09 (25.71)	10 (28.57)	09 (25.71)	06 (17.14)	34 (24.29)
B n (%)	10 (28.57)	14 (40.00)	12 (34.29)	**25 (71.43)**	61 (43.57)
AB n (%)	07 (20.00)	05 (14.29)	06 (17.14)	02 (5.71)	20 (14.29)
O n (%)	09 (25.71)	06 (17.14)	08 (22.86)	02 (5.71)	25 (17.86)
Total n (%)	35 (100.00)	35 (100.00)	35 (100.00)	35 (100.00)	140 (100.00)
Chi-square test	$\chi^2 = 17.295$, df = 9, P = 0.044 (<0.05), **Significant**				

DISCUSSION

The realm of human genetics extends far beyond merely studying inherited diseases. It has transformed into a pivotal biological field, investigating how inherent factors intersect with environmental influences.

The ABO blood group system is a classification of human blood based on the presence or absence of two antigens, A and B, on the surface of RBCs. ABO antigens are not confined to RBCs only, infect they are found on epithelial cells of various tissues such as mucosa and body fluids as well.[5] They can also be present on key receptors such as EGF receptors, integrins, cadherins and CD-44 cells, which control cell proliferation, adhesion and motility.[6] Several investigators studied that ABO antigens are associated with the risk of carcinogenesis and could be crucial for identifying personalized oncogenic risk factors. Several hypotheses have been proposed suggesting role of ABO blood group in cancer pathophysiology that offer insights into a few potential mechanisms as follows:-

1. Inflammatory Responses:

Blood group antigens can influence the production and secretion of cytokines and chemokines, which are signaling molecules involved in inflammatory responses. Variations in blood groups may lead to differences in the expression of these mediators; affecting the inflammatory milieu and influencing cancer development.[7]

Recent studies reported an association between polymorphisms at the *ABO* gene locus and circulating levels of tumor necrosis factor-alpha[8], soluble intercellular adhesion molecule (ICAM)-1.[9,10], E-selectin.[11, 12]and P-selectin.[10] All these adhesion molecules are important mediators of chronic inflammation and directly influence tumor initiation and spread.[13]

2. Genetic and Molecular Pathways:

One plausible hypothesis encompasses a dysregulation of the enzymatic activity of the ABO glycosyltransferases, which are specifically involved in the processes of intercellular adhesion and cellular membrane signaling as well as in the immune response to the host. [14, 15] The alteration of these surface molecules may promote the process of malignancy.[16] ABO glycosyltransferases modulate the circulating plasma levels of von Willebrand factor which was recently found to be an important modulator of angiogenesis and apoptosis, which, in turn, are processes involved in tumorigenesis. [17,18]

3**. Blood Group Antigens on Tumor Cells:**

The H antigen is a precursor for A and B antigens. One widely-occurring change observed in a large variety of human cancer is deletion of A or B epitope, associated with accumulation of their precursor H which causes enhanced malignancy.

It is important to note that the understanding of these mechanisms is still evolving and further research, including molecular and genetic studies, is needed to unravel the intricate connections between ABO blood groups and the development of oral cancers and dysplasia. Our research revealed a link between ABO blood groups and the development of PMDs and oral cancer, particularly in individuals who chew Gutkha, Zarda, or smoke. Most studies report a predominance of blood group A or B in cancer cases. Our findings indicate that individuals with blood group B are more prone to oral cancer, likely due to antigen presence on epithelial cells, including the oral mucosa. In blood groups A and B, H antigen converts to A and B antigens; in blood group O, it remains unchanged. Thus, O group individuals, having the most H antigen, are protected against oral cancer.

Among the cases of OSMF, the male-to-female ratio was 2:1, mostly observed in ages 21-40 years, consistent with Gheena & Jain [19] and Siddique S *et al*.[20] Gutkha consumption was prevalent in 88.57% of cases, indicating supari/areca as a primary cause. Among OSMF cases, 40% of subjects had blood group B, followed by A>O>AB, but this was not statistically significant. Similar findings were reported by Siddique S *et al*. [20] and Mahalakshmi *et al*. [21] In another study by Vaish *et al*, [22] blood group A individuals are also vulnerable to OSMF and Oral Lichen Planus.

Among the cases of leukoplakia, male-to-female ratio was 3.4:1, mostly affected age being 51-60 years. 71% patients were using smokeless form of tobacco while 29% smoked. Although a definitive association between ABO blood group and leukoplakia was not observed, it is worth noting that 34% of subjects belonged to the B blood group followed by A>O>AB . However, this distribution did not demonstrate statistical significance. Contrarily, Bhateja S and Arora G[23] revealed the predominance with significant grades of dysplasia belongs to blood group A in both Leukoplakia and OSMF cases.

In present study, among oral cancer cases, male female ratio was 3:2 with highest occurrence observed among individuals aged 31-60. This was in accordance to study done by Mortazavi H *et al*.[6] Our study showed 85.71% of oral cancer patients chewed tobacco across all blood groups, despite of which individuals with blood group B had a higher incidence (71.43%) of oral cancer. Akhtar *et al*,[24] also showed a high incidence of blood group B (37.5%), in

patients with oral cancer. The individuals with B antigens showed increased resistance to apoptosis; these play a vital role in carcinogenesis which probably explains the increase risk of individuals with B blood group, to develop more affinity for oral cancer. [25]

Contrarily, Jaleel in another study on Indian population, showed that people with blood group A had 1.4 times higher risk of developing oral cancer followed by B blood group (1.1 times), AB (0.9 times) and O (0.6 times). [26] Tyagi SP *et al* [27]; Mittal VP and Gupta S [28]; Nayak SK [29] and Baruah BD & Gogoi BC [30] also reported predisposition of blood group A for oral cancer.

We observed the relative frequencies of the ABO blood groups in oral precancer and oral cancer has the strongest association with blood group "B" But the racial and ethnic distribution of blood groups and size of sample is an important factor for predicting the cancer risk.

CONCLUSION:

Our research shows heightened **correlation between blood group B and susceptibility to the development of oral cancer** as **71.43%** were found to have **blood group B**. This revelation highlights the importance of considering ABO blood group as a potential risk factor in malignant transformation of OPMDs and in early assessment of oral cancer.

IMPLICATIONS FOR PERSONALIZED RISK ASSESSMENT:

Discovering a correlation between a specific blood group and cancer occurrence could revolutionize preventive healthcare. This knowledge might prompt lifestyle changes that may reduce disease incidence and accurate guidance from healthcare professionals for informed decisions about individual well-being.

LIMITATIONS:

Main limitation was a small sample size, insufficient to represent disease prevalence and various environmental influences globally. Our study excluded salivary gland and other soft-tissue malignancies in the maxillofacial region, despite their prevalence in tobacco and areca nut users.

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CONFLICTS OF INTEREST- No conflicts of interest

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