Original Article - Retrospective Study

ABO Blood Groups as Predictors of Oral Malignancy Risk - A Retrospective Study

Abhilasha Yadav[1,2], Anuj Jain[3,4], Rajiv Borle[2], Bindu Singh[2]

[1]Department of Oral and Maxillofacial Surgery, Government Dental College and Hospital, Mumbai, [2]Department of Oral and Maxillofacial Surgery, Sharad Pawar Dental College, Datta Meghe Institute of Higher Education, Sawangi (Meghe), Wardha, [4]Department of Dental Research Cell, Dr. D. Y. Patil Dental College and Hospital, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, [3]Department of Oral and Maxillofacial Surgery, Narsinhbhai Patel Dental College and Hospital, Sankalchand Patel University, Visnagar, Gujarat, India

Abstract

Introduction: Oral cancer is a major public health issue globally, especially in developing countries. While various risk factors for oral malignancies have been identified, the role of genetic and immunological predisposition remains unclear. This retrospective case–control study investigates the association between ABO blood groups and the risk of developing oral malignancies in the Indian population, aiming to provide insights into potential predictive markers for early detection and prevention. **Materials and Methods:** A total of 307 patients with histologically confirmed oral malignancies, diagnosed between January 2011 and December 2014, were analysed. Demographic details, ABO blood group data and the anatomical site of malignancy were extracted from medical records. These patients were compared to 600 healthy controls. Statistical analysis used the Chi-square test for association, and odds ratios were calculated to estimate risk. **Results:** Among 307 patients diagnosed with oral malignancies, the majority were male (75%), with the peak incidence observed in the fifth decade of life. Buccal mucosa was the most commonly affected site (73%), followed by tongue and alveolar ridge. Analysis of ABO blood group distribution revealed that blood group A was the most prevalent among cases. Individuals with blood group A demonstrated a 1.46-fold higher risk of developing oral malignancies compared to other blood groups ($P < 0.05$). **Discussion:** The study showed a significant association between blood group A and the risk of developing oral malignancies in the Indian population. These findings may assist in identifying high-risk individuals and developing targeted screening programs for early detection and improved outcomes.

Keywords: ABO blood group, oral malignancy, oral squamous cell carcinoma, predictive marker, risk factor

Introduction

Head-and-neck cancers encompass malignancies occurring in the oral cavity, sinonasal cavity, pharynx, larynx and other related regions.[1] Oral cancer represents a significant health burden, particularly in countries like India, where it accounts for a substantial proportion of cancer cases diagnosed annually. According to GLOBOCAN 2020, malignant neoplasms accounted for an estimated 19.3 million new cancer cases and 10 million cancer-related deaths worldwide in 2020, underscoring the growing global burden of cancer.[2] Although oral cancers account for a relatively small proportion of all cancer cases globally, they are notably more common among males, ranking as the sixth most frequent cancer in men and fifteenth among women worldwide.[2] In India, oral cancer represents one of the leading causes of cancer morbidity and mortality, largely attributable to widespread habits such as tobacco chewing, smoking and alcohol consumption.

The aetiopathogenesis of oral malignancies is complex and multi-factorial, involving both environmental exposures and intrinsic factors such as genetic predisposition and immunological background. Known risk factors include tobacco and betel quid usage, alcohol consumption, poor oral

Access this article online

Quick Response Code:

Website: https://journals.lww.com/aoms

DOI: 10.4103/ams.ams_33_25

Address for correspondence: Dr. Abhilasha Yadav, Department of Oral and Maxillofacial Surgery, Government Dental College and Hospital, Mumbai, Maharashtra, India. E-mail: drabhilasha@yahoo.com

Received: 02-03-2025 **Last Revised:** 24-06-2025
Accepted: 05-08-2025 **Published:** 27-10-2025

How to cite this article: Yadav A, Jain A, Borle R, Singh B. ABO blood groups as predictors of oral malignancy risk - A retrospective study. Ann Maxillofac Surg 0;0:0.

hygiene, viral infections like human papillomavirus (HPV), dietary deficiencies and genetic susceptibility.[3,4] However, even with the elimination of external carcinogens, some individuals continue to develop oral cancer, suggesting the involvement of other inherent biological factors.[3,4]

The ABO blood group system, discovered by Karl Landsteiner in 1901,[5] has long been studied for its potential associations with various disease processes. Beyond its importance in transfusion medicine, ABO blood group antigens have been implicated in susceptibility to infections, cardiovascular diseases and several malignancies. Numerous studies have highlighted the association of the ABO blood group system with various infectious and non-infectious disease, including various malignancies.[6-9] Since the early 20th century, researchers have speculated on a possible link between ABO blood groups and various malignancies, including those of the oral cavity.[6] Subsequent studies have investigated the relationship between ABO blood groups and various cancers, including gastric, pancreatic, breast and oral cancers.[10-12]

Materials and Methods

This study employed a retrospective case–control design to evaluate the association between ABO blood groups and the risk of developing oral malignancies. The study was conducted at a tertiary care centre in central India, over a 4-year period from January 2011 to December 2014, after obtaining the approval from the institutional ethics committee with Reference No. DMIMD (DU)/IEC/2014-15/1122 dated 30 December 2014. This retrospective study was approved by the institutional ethics committee for the use of anonymised patient data recorded between 2011 and 2014. As the study involved no direct patient interaction or intervention and utilised de-identified medical records, the requirement for informed consent was waived by the ethics committee in accordance with institutional policy and ethical guidelines for retrospective research. The study adhered to the ethical principles outlined in the Declaration of Helsinki (2013 revision).

The case group comprised 307 patients who were histopathologically confirmed to have oral malignancies. Data, including age, sex, ABO blood group and the anatomical site of malignancy, were extracted from institutional medical records. The control group consisted of 600 voluntary blood donors who had no history of malignancy or significant systemic illnesses and whose ABO blood group data were recorded during routine blood donation activities. The control group enabled a baseline comparison of ABO blood group distribution in the general population. This allowed for the identification of any significant deviations in blood group prevalence among oral malignancy patients, thereby serving as a critical reference to assess the strength of association between blood group type and cancer risk.

Inclusion criteria for cases included all patients aged 18 years and above with histopathologically confirmed malignancies of the oral cavity (ICD-10 codes C00–C06) diagnosed between 2011 and 2014. Sites comprised the buccal mucosa, tongue, alveolar ridge, retromolar trigone, floor of the mouth and other intraoral locations. Minor salivary gland tumours within the oral cavity were included if confirmed malignant. TNM staging data were not consistently available across all records and were therefore excluded to maintain dataset uniformity. Exclusion criteria included recurrent oral cancers, secondary malignancies and incomplete medical records. Pharyngeal malignancies (e.g., oropharynx and hypopharynx) and major salivary gland tumours (e.g., parotid and submandibular) were excluded.

The study aimed to investigate the association between ABO blood groups and oral malignancies, with ABO blood group as the primary independent variable and oral malignancy status as the primary dependent variable. Secondary variables included age, gender, tobacco use, alcohol consumption, dietary habits, socioeconomic status and the site of malignancy, all of which were considered to provide further insight into the risk factors for oral cancer. Potential confounding variables, such as tobacco use, alcohol consumption, genetic predisposition, age and gender, were controlled for using stratified analysis. Socioeconomic status was approximated using available data on patient occupation and residential locality. Patients were broadly categorised into low, middle and high SES groups; however, due to incomplete records, SES was not used in statistical comparisons.

The diagnostic criteria for oral malignancy were based on histopathological confirmation of malignancy from biopsy samples, categorised according to the World Health Organization classification of head-and-neck tumours.[13] These variables were carefully documented to ensure accurate analysis and minimise the impact of confounding factors on the study's results.

The primary outcome measure was the association between ABO blood groups and oral malignancy risk. Secondary outcomes included demographic distribution and site-specific involvement. Blood grouping was performed using the standard slide agglutination method. In this technique, a drop of the subject's blood is mixed with commercially prepared monoclonal anti-A, anti-B and anti-D sera on a clean glass slide. The presence or absence of visible agglutination is used to determine the ABO and Rh blood group. This method is widely used due to its simplicity, accuracy and rapid results. While Rh (D) typing was conducted routinely, only ABO group data were used for statistical analysis in this study.

The sample size included all eligible patients diagnosed during the study period, ensuring adequate power for statistical comparisons. Statistical analysis was performed using Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS), version 17.0 (SPSS Inc., Chicago, IL, USA). The Chi-square test was used to assess the association between ABO blood groups and oral malignancy. Odds ratios (OR) and 95% confidence intervals (CI) were calculated to estimate the strength of association. $P \leq 0.05$ was considered statistically significant.

Results

A total of 307 patients diagnosed with oral malignancy were included in the study, of which 229 (75%) were males and 78 (25%) were females, yielding a male-to-female ratio of approximately 3:1. The mean age of patients was 46 ± 5 years, with a peak incidence observed in the fifth decade of life (41–50 years, 27%), followed closely by the sixth (51–60 years, 24%) and fourth decades (31–40 years, 18%) [Figure 1]. The mean age of male patients was 53.2 ± 4 years, while the mean age of female patients was 40.4 ± 3 years. Histopathological examination revealed that 84% of the cases were oral squamous cell carcinoma, followed by verrucous carcinoma (9%) and minor salivary gland tumours (7%) [Table 1].

Regarding the anatomical site of malignancy, the buccal mucosa was the most commonly affected site, accounting for 73% of cases, followed by the tongue (15%), alveolar ridge (7%) and other sites (5%) such as the floor of the mouth and palate [Figure 2]. This distribution is reflective of the common habit patterns in the studied population, particularly smokeless tobacco use affecting the buccal mucosa. A subgroup analysis indicated that blood group A was most commonly associated with malignancies of the buccal mucosa, the predominant anatomical site in our cohort. However, due to smaller sample sizes for other sites such as the tongue and alveolar ridge, the statistical significance of blood group-site associations could not be reliably established and warrants further investigation in larger cohorts.

Analysis of blood group distribution among cases revealed that blood group A was the most prevalent (38%), followed by blood group B (31%), blood group O (24%) and blood group AB (7%). In contrast, among the control group, blood group O was the most common (49%), followed by blood groups B (27%), A (18%) and AB (6%) [Table 2].

Statistical analysis demonstrated a significant association between blood group A and oral malignancy ($P < 0.05$). Odds ratio analysis revealed that individuals with blood group A had a 1.46-fold increased risk of developing oral malignancies (OR = 1.46, 95% CI: 0.85–1.66), while blood group B had a slightly elevated but statistically non-significant risk (OR = 1.12, 95% CI: 0.78–1.34). Blood group AB also showed no significant association (OR = 0.98, 95% CI: 0.62–1.24). In contrast, blood group O demonstrated a potential protective effect with a lower risk (OR = 0.68, 95% CI: 0.52–0.88) [Table 3].

Gender-specific analysis indicated that among male patients, blood group A was the most commonly observed, and a similar trend was noted among female patients, although to a lesser extent [Figure 3].

Table 1: Distribution of oral malignancy types among cases

Type of malignancy	Frequency, *n* (%)
Oral squamous cell carcinoma	258 (84)
Verrucous carcinoma	28 (9)
Minor salivary gland tumours	21 (7)
Total	307 (100)

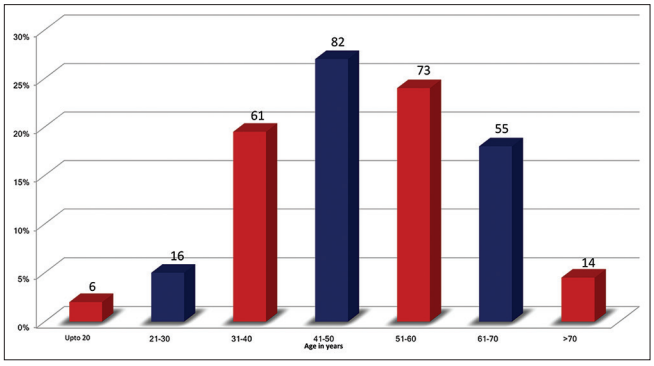

Figure 1: Agewise distribution of subjects

Discussion

This retrospective case-control study evaluated the association between ABO blood groups and the risk of developing oral malignancies in the central Indian population. Our findings indicate that individuals with blood group A have a significantly higher risk of oral malignancy, while blood group O appears to exert a protective effect. These results highlight the potential of ABO blood typing as a low-cost, non-invasive tool in oral cancer risk stratification.

Our findings are in agreement with previous studies conducted by Verma *et al*.,[14] Raghavan *et al*.,[15] Mittal and Gupta,[16] Jaleel and Nagarajappa,[17] and Shishodia *et al*.,[18] who reported an increased risk of oral malignancy in individuals with blood group A. A meta-analysis by Singh and Purohit[19] also supports this association, concluding that blood group A is linked with an elevated risk of oral cancer and oral potentially malignant disorders. These studies suggest that blood group antigens, which are expressed on epithelial cells, including the oral mucosa, may play a role in modulating immune responses or influencing carcinogenesis.

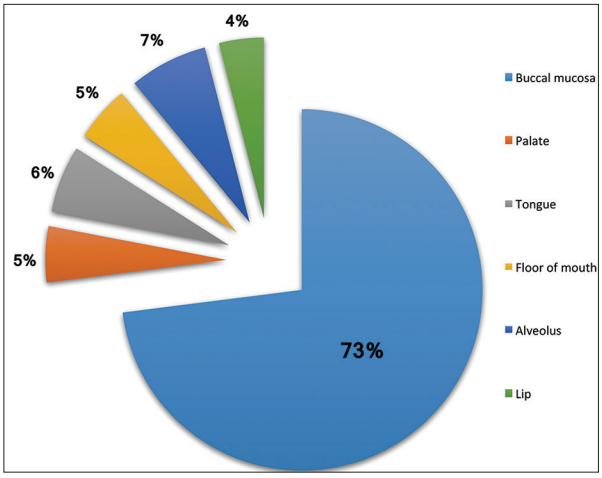

Figure 2: Sitewise distribution of subjects

Table 2: Distribution of blood groups in study subjects and controls

Blood group	Patients with oral cancer, *n* (%)	Controls, *n* (%)	*P*
A	117 (38)	174 (29)	0.04 (significant)
B	62 (20)	90 (15)	0.08 (NS)
AB	30 (10)	40 (7)	0.27 (NS)
O	98 (32)	296 (49)	0.02 (significant)
Total	307 (100)	600 (100)	

NS: Non-significant

Table 3: Strength of association between ABO blood groups and oral cancer

Blood group	OR	95% CI	Interpretation
A	1.46	0.85–1.66	Higher risk
B	1.12	0.78–1.34	No significant association
AB	0.98	0.62–1.24	No significant association
O	0.68	0.52–0.88	Protective effect

OR: Odds ratio, CI: Confidence interval

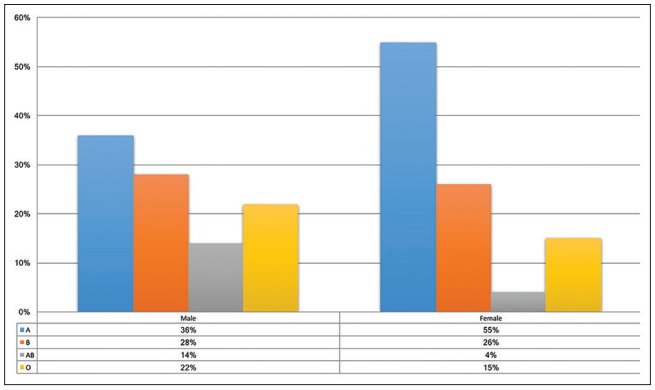

Figure 3: Relationship of ABO blood groups with gender of the affected patients

In contrast, our analysis demonstrated that blood group O is associated with a lower risk of oral cancer, a finding supported by the same meta-analysis and several other studies. This protective effect may be due to the preservation of the H antigen in individuals with blood group O, which is not converted into A or B antigens. Some studies hypothesise that the lack of A and B antigens may reduce malignant transformation by limiting abnormal cell adhesion or immune escape.[20]

Studies with conflicting results, such as those by Mortazavi *et al*.,[6] Sharma *et al*.,[21] Ghooi *et al*.,[22] and Mahalakshmi *et al*.,[23] suggested a higher susceptibility among individuals with blood group B. In addition, Tyagi *et al*.,[12] found no significant association between blood group and oral cancer risk. These discrepancies could be attributed to differences in sample size, regional population genetics, lifestyle factors or methodology, further emphasising the need for larger multi-centre trials.

Our data also revealed a predominance of oral malignancies among male patients, with peak incidence in the fifth decade of life. This finding is consistent with global trends reported by Chow[1] and Sung *et al*.,[2] and may be explained by greater exposure of men to risk factors such as tobacco, alcohol and occupational hazards. Furthermore, the most commonly affected site in our cohort was the buccal mucosa, which aligns with the habitual use of smokeless tobacco in the study population.[24]

A meta-analysis of observational studies by Shi *et al*.,[25] also suggests that a correlation exists between ABO blood groups and tumours in the head-and-neck region. However, the link between blood type and head-and-neck tumours requires further confirmation through more prospective studies.

The main strength of this study lies in its relatively large sample size and clearly defined inclusion criteria. However, being a retrospective, single-centre study, it is subject to inherent limitations such as potential selection bias. In addition, behavioural risk factors such as tobacco or alcohol consumption were not uniformly recorded in the medical records, limiting the ability to control for these confounders in multi-variate analyses. As a retrospective epidemiological study, this investigation does not include molecular or mechanistic data to explain the biological link between ABO blood groups and oral malignancy. Future studies incorporating genomic and immunological markers are warranted to build upon these epidemiological observations.

Behavioural risk factors such as betel nut chewing, tobacco use and alcohol consumption were not consistently documented in patient records and were therefore not included in the analysis. Likewise, viral aetiologies such as HPV infection were not tested or recorded. These represent important limitations, and future studies should aim to incorporate comprehensive risk factor profiling and biomarker analysis.

Despite these limitations, our study contributes valuable data to the understanding of host-related factors in oral cancer. As a genetically determined trait, ABO blood group typing could serve as a supplemental screening tool in high-risk populations. Future research should aim to incorporate molecular and immunological assays to elucidate the mechanisms linking ABO antigens and oral carcinogenesis and to confirm these associations in prospective, multi-regional cohorts.

Conclusion

This study demonstrates a significant association between ABO blood group A and an increased risk of developing oral malignancies in the central Indian population. These findings suggest that ABO blood typing may serve as an additional risk stratification tool to identify individuals at higher risk for oral cancer. Public health efforts should emphasise early screening, particularly among males over 40 years of age with blood group A, to facilitate early diagnosis and improve clinical outcomes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Chow LQ. Head and neck cancer. N Engl J Med 2020;382:60-72.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209-49.
3. Jasim A, Li X, Octavia A, Gunardi I, Crocombe L, Sari EF. The association between betel quid use and oral potentially malignant and malignant disorders in Southeast Asian and Pacific regions: A systematic review and meta-analysis with GRADE evidence profile. Front Oral Health 2024;5:1397179.
4. Mahuli AV, Sagar V, Kumar A, Mahuli SA, Kujur A. A systematic review and meta-analysis assessing the role of oral health as a risk factor in oral cancer. Cureus 2023;15:e39786.
5. Mohd Noor NH, Siti Asmaa MJ. Karl Landsteiner (1868-1943): A versatile blood scientist. Cureus 2024;16:e68903.
6. Mortazavi H, Hajian S, Fadavi E, Sabour S, Baharvand M, Bakhtiari S. ABO blood groups in oral cancer: A first case-control study in a defined group of Iranian patients. Asian Pac J Cancer Prev 2014;15:1415-8.
7. Abegaz SB. Human ABO blood groups and their associations with different diseases. Biomed Res Int 2021;2021:6629060.
8. Jing W, Zhao S, Liu J, Liu M. ABO blood groups and hepatitis B virus infection: A systematic review and meta-analysis. BMJ Open 2020;10:e034114.
9. Ward SE, O'Sullivan JM, O'Donnell JS. The relationship between ABO blood group, von Willebrand factor, and primary hemostasis. Blood 2020;136:2864-74.
10. Cui H, Qu Y, Zhang L, Zhang W, Yan P, Yang C, *et al*. Epidemiological and genetic evidence for the relationship between ABO blood group and human cancer. Int J Cancer 2023;153:320-30.
11. Greer JB, Yazer MH, Raval JS, Barmada MM, Brand RE, Whitcomb DC. Significant association between ABO blood group and pancreatic cancer. World J Gastroenterol 2010;16:5588-91.
12. Tyagi SP, Pradhan S, Agarwal SS. Blood groups in malignant diseases. J Indian Med Assoc 1965;45:645-50.
13. El-Naggar AK, Chan JK, Takata T, Grandis JR, Slootweg PJ. The fourth edition of the head and neck World Health Organization blue book: Editors' perspectives. Hum Pathol 2017;66:10-2.
14. Verma P, Kumar A, Dixit S, Mohan K, Gupta N, Mandal G. Assessment of relationship of ABO blood groups in oral cancer patients – A retrospective study. Ann Maxillofac Surg 2021;11:80-5.
15. Raghavan VM, Bailoor DN, Jhansirani P. Incidence of ABO blood groups in oral cancer in South Kanara District. J Indian Dent Assoc 1986;58:305-8.
16. Mittal VP, Gupta S. The study of ABO blood groups in oral cancer. J Cancer 1969;6:34-7.
17. Jaleel BF, Nagarajappa R. Relationship between ABO blood groups and oral cancer. Indian J Dent Res 2012;23:7-10.
18. Shishodia NP, Anekar J, Raj AC, Jhugroo C, Divakar DD, Alshehri SZ, *et al*. Insight on the relationship of ABO blood grouping associated with oral premalignant lesions, conditions and inherited oral cancer syndromes. J Exp Ther Oncol 2019;13:59-63.
19. Singh A, Purohit BM. ABO blood groups and its association with oral cancer, oral potentially malignant disorders and oral submucous fibrosis- a systematic review and meta-analysis. Asian Pac J Cancer Prev 2021;22:1703-12.
20. Auclair PL. Altered H-antigen reactivity as an early indicator of malignant transformation in oral epithelium. J Oral Pathol 1984;13:401-11.
21. Sharma G, Choudhary R, Bharti D. Studies showing the relationship between ABO blood groups and major types of cancer. Asian J Exp Sci 2007;21:129-32.
22. Ghooi AM, Kamalpuria SK, Jain PK, Tandon PL. Distribution of blood groups in cancer. Indian J Cancer 1970;7:296-305.
23. Mahalakshmi IP, Sinha P, Nagaraj T, Okade D, Nonitha S, Veerabasaivaiah BT. Relationship between ABO blood group and Rh factor with oral potentially malignant disorder. J Oral Maxillofac Pathol 2022;26:57-9.
24. Kadashetti V, Shivakumar KM, Choudhary M, Patil S, Gawnde M. Awareness and knowledge of tobacco associated risk of development of oral cancer and oral potentially malignant disorders among patients visiting a dental college. J Family Med Prim Care 2020;9:2244-7.
25. Shi H, Yao J, Jiang C, Xu W, Jiang Z, Chen Y, *et al*. ABO blood types and head and neck cancer: A systematic review with meta-analysis of observational studies. BMJ Open 2024;14:e088016.