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BLOOD GROUP SYSTEM- A RISK INDICATOR OF ORAL CANCER

Oral Pathology

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ABSTRACT

The Red blood cell surface predominantly contains antigens for ABO blood group. These antigens are present also in several epithelial cells such as esophagus, salivary glands. Numerous research have been conducted to identify a specific, reliable biomarker, which can distinguish oral cancer patients from healthy individuals and also to identify patients with high risk oral premalignant lesions. It is hypothesized that majority of human cancers are epithelial cells derivatives hence changes in blood group antigens may play a key role by expressing certain blood group carbohydrate antigens on the surface of cancer cells regarded as a result of tumor formation or production that can be used as a reliable prognostic marker. The aim of the present review is to establish the role of ABO blood group as a confounding factor in early oral cancer detection in order to obtain a diagnosis for better management of patients with oral precancerous lesions/conditions.

KEYWORDS

Oral cancer; cell surface antigens; gene expression; cell adhesion

INTRODUCTION:-

A sudden rise in death rate frequency since last two decades due to oral cancer have increased the efforts required to create awareness as well as to identify new diagnostic methods to support better treatment modalities to fight against this-life threatening disease. Oral cancer is 5th most common cancer worldwide and apparently the most common malignancy after the cervical and stomach cancer in developing countries. The predictable risk factors for oral squamous cell carcinoma (OSCC) include smoking, tobacco chewing, and consumption of alcohol. Various confounding risk factors are exposure to either physical, chemical carcinogens such as food preservatives, phenols, air pollutants and hazardous radiations such as UV and X-ray radiation. Certain infectious conditions such as syphilis, infection with human papilloma virus (HPV) or Candida albicans and malnutrition are also believed to play a vital role in progression of OSCC[1, 2]. Lipid or glycolipids or glycoproteins found on cellular membrane often undergo some changes during cell maturation or malignant transformation. Most of the time, the outer part of such glycoconjugates consist of carbohydrates like ABO and Lewis blood group antigens. High incidences of various oral carcinomas are found in patients having A/B blood groups. Numerous mechanisms have been proposed to explain the association between ABO blood groups and risk of cancer such as inflammation, cell to cell adhesion and membrane signaling.[3] Analyses of ABO blood group immunohisto chemically have demonstrated loss of expression of A or B antigens in more than 80% of patients with OSCC. Correspondingly, potentially malignant lesions expressing epithelial dysplasia have also shown loss of expression of these antigens [4].

MECHANISM AND MOLECULAR ORIGIN:-

a)Concept of epitope:-

More than 20 genetically determined blood group systems are identified among various studies conducted till date but ABO blood groups are sensitive than other blood grouping system. ABO blood group system comprising of 4 blood groups namely O, A, B, and AB. The distribution diverges in dissimilar geographic and ethnic individuals, and socioeconomic groups. These blood group antigens are chiefly alloantigens in humans presenting on the external surface of red blood cells by a cell surface receptor and various other epithelial cells like esophagus, salivary gland. Complete or partial absence of A or B epitope has been reported in many cancers which are related with the increase in precursor component of the epitope which causes enhanced malignancy, although the molecular genetic mechanism leading to such phenotypic changes is not known. The ABO blood group genes are mapped to 9q region where it is assumed that most common genetic alterations of cancers are mapped at 9q34.2 region [5, 6]. Thus expression of significant blood group carbohydrate antigens on the surface of cancer cells may be influenced directly or indirectly by genetic change of proliferative malignant cells, the loss or presence of blood group antigens can increase cellular motility or facilitate the interface between tumor cells and endothelial cells during metastasis of proliferative cells to distant organs which are reflected as an end product of tumor progression in tumorigenesis that can be used as useful prognostic and diagnostic markers [7].

b)Adhesion and progression:-

The association with blood groups and incidence, clinicopathological conditions and treatment outcome had been studied in many systemic cancers such as stomach, breast, skin, cardiac, lungs, colorectal. The association between esophageal carcinoma with “A” blood group was first discovered by Arid and Bentall in 1953. In the literature previous studies have shown blood group "A" was significantly more common in patients with gastric, laryngeal, hypopharynx, pancreatic, breast, testicular, and bone cancers. Studies also have shown the relationship between blood group "A" and gastric carcinoma [8]. Juvanovic-Cupic et al stated that blood type B was more prevalent in patients with oral and gastrointestinal cancers. The hypothesis behind such correlation in various studies is owing to the malignant cells produce an antigen immunologically related to blood group "A" antigen but blood group "O" antigens may have a non-proliferative effect by preventing the growth and spread of the tumor. Because of this resemblance, antibodies to "A" blood group most likely to attack premalignant and uncontrollable proliferative cells expressing this antigen. The loss of blood antigens result in the tumor cells acquisition the ability to move and circulate through the body as antigens loss the ability to express integrins, a cell adhesion protein which typically express an A like antigen on their receptor and control cell movement. The homotypic and heterotypic cell adhesion mediated by interactions of certain blood group carbohydrates with analogous lectins is a decisive process at the extravasation step of the metastatic cancer cells from the circulatory pathway to the distant site during metastatic cascade of secondary tumor growth[9, 10].

c)T and Tn antigens:-

Malignant breast cells or esophageal cells develop a tumor marker called Thomsen- Friedenrich (T) antigen, which is dormant or inactive in normal healthy cells. Tn antigen (precursor of T antigen) only becomes activated as a cell become malignant. T and Tn antigens show some structural resemblance to “A” antigen. Blood group “A” individuals have the minimum antagonistic antibody immune response against the T and Tn antigens and they are truly immunologically considered similar because of their mutual terminal sugar (N-acetylgalactosamine). Individuals with A blood group have the most prominent, higher and uniform suppression of the level of Tn antigens, irrespective of age, cancer stage, or tumor morphology and lower level of anti-B-isohemagglutinnins may contribute to the poorer

prognosis even after complete therapy in many cancers including oral and paraoral regions[11].

Risk predictability in oral cancer:

Etiology of oral cancer is influenced by natural life style modifications along with genetic and hereditary effects. The ABO blood group is one such genetic factor that is thought to be associated with oral cancer. In oral cavity various studies have shown small association between blood group "A" and cancer development involving salivary gland, pharyngeal and laryngeal region. The H antigen present in all individual blood groups is believed to be the precursor antigen for the development of A and B antigens. Individuals with A and B blood groups, the precursor H antigen is converted to A and B antigen correspondingly and those having O blood group have the highest amount of H antigen, which is thought to offer defense against oral cancers. Individuals with blood group “A” are anticipated to be at a higher risk for developing oral cancer due to the expression of an A-like antigen (Forssmann or Tn antigen). The so- called 'incompatible “A” expression' was detected in cancer. Malignant cells are expresses A antigen even in individuals with blood group B or O. Thus antibodies to A can target precancerous and cancerous cells. Individuals with blood groups A and AB lack antibodies to A and are thus more likely to develop oral cancer [12, 13, 14].

Ramesh et al in his review on association of blood group with oral cancer concluded that an inherited component plays a key role in susceptibility or resistance to various types of cancers. It is also found that prediction of the risk of cancer depends on racial and ethnic distribution of blood groups.[15] A Study conducted by Bhateja et al has shown the frequency of blood group "A" was predominant in both leukoplakia and OSMF group. Blood group "A" individuals appear to be at a reasonably increased risk for many cancers arising from oral and paraoral regions. Deletion or reduction of blood group A or B antigen in tumors of A or B individuals is associated with the degree of malignancy and metastatic potential in many types of oral cancers. The individuals with blood groups A and AB failed to present antibodies to A and hence are more prone to develop tumors of epithelial origin. Similar study has also shown blood group "A" significant number of precancerous patients with severe dysplasia than other blood groups [16].

Sharma et al observed a significant correlation between breast cancer and blood type A. Also, they reported that the frequency of blood types B and O was equally higher than other blood types in patients with cervical cancer. The blood type B was more common in patients with oral mucosal cancer [17]. Jaleel et al illustrated individuals with “A” blood group type have 1.46 times higher risk of developing oral cancer than other blood groups. He concluded that occurrence of A and B antigens on cells may increase the risk of OSCC. [18] According to Xie et al the correlation of blood type and risk of cancer varies according to origin, race and several environmental factors. He also observed that tumor formation, progression and metastases are commonly associated with a downregulation of glycosyl transferase, predominant enzyme involved in the biosynthesis of A and B antigens. Partial or complete deletion of epithelial blood group antigens due to anomalies or any signal detection failures during their synthesis results in altered cell surface. This altered antigen pattern on the cell surface is a tumor related modification observed in malignancies. [19]

Biondi et al reported greater incidence of blood type O among patients with oral cancer. The protective effect of blood group O on cancer progression is owing to increased apoptosis resistance of epithelial cells presenting A and B antigens. The study illustrated ABO antigens can also be present on vital receptors such as EGF receptors, integrins , cadherins and CD-44, which control cell proliferation, adhesion and motility. The role of ABO antigens in tumorigenesis may be altered as the expression patterns of these receptors vary in normal and cancerous cells. [20, 21]

Study conducted by Mortazavi et al demonstrated that oral cancer patients had significantly lower frequency of blood type O and higher frequency of blood type and also associated squamous cell and non-squamous cell cancers and described higher frequency of blood type B in patients with non-squamous cell cancer. [22] Gopal Reddy et al reported that blood group A patients had increased risk of developing oral submucous fibrosis, the most prevalent potentially malignant condition among the Indian population [23]. Saxena et al assessed the relationship of blood group with oral cancer in Western Rajasthan and found that blood group A had the strongest association with oral cancer followed by blood types O and B. [24].

CONCLUSION:-

A need for better risk assessment tool is important to diagnose oral cancer in its early stages, since the management of benign or localized tumors includes less morbidity and mortality than more advanced-stage disease involving metastases, lymph nodal spread where treatment must be more aggressive. From the above review it is undoubtedly that blood grouping can be used as a routine method to detect the susceptible individuals with OSCC and counsel them to minimize the risk factors such as smoking, alcohol consumption and other precipitating factors. It should be also noted that regular cancer screening should be planned for those individuals with greater susceptibility. Future studies by using advanced molecular methods have to be conducted to identify the exact association between ABO and oral cancer across different geographical areas to obtain a better understanding of susceptibility. Certainly, the stage in which the disease is detected is directly correlated to long-term existence or survival of an individual.

REFERENCES:-

1) Vigneswaran N, Williams MD. Epidemiologic trends in head and neck cancer and aids in diagnosis. Oral Maxillofac Surg Clin North Am 2014;26(2):123-41.
2) Cerovic R, Juretic M, Balen S, Belusic M, Caser L, Rogic M. Examining the presence of ABO (H) antigens of blood types in the saliva of patients with oral cancer. Coll Antropol 2008;32(2):509-12.
3) Hakomori S. Structure, organization and function of glycosphingolipids in membrane. Current Opnin Hematology. 2003;10:16-24.
4) Gao S, Bennett EP, Reibel J, ChenX, Christensen ME, Krogdahi A et al. Histo-blood group ABO antigen in oral potentially malignant lesions and squamous cell carcinoma-genotypic and phenotypic characterization. APMIS 2004;112(1):11-20.
5) Pack SD, Karkera JD, Zhuang Z, Pak ED, Balan KV, Hwu P, et al. Molecular cytogenetic fingerprinting of esophageal squamous cell carcinoma by comparative genomic hybridization reveals a consistent pattern of chromosomal alterations. Genes Chromosomes Cancer 1999;25:160-68.
6) Simoneau M, La Rue H, Aboulkassim TO, Meyer F, Moore L, Fadet Y. Chromosome 9 deletions and recurrence of superficial bladder cancer identification of four regions of prognostic interest. Oncogene 2000;19:6317-23.
7) Ichikawa D, Handa K, Hakomori S. Histo blood group AB antigen deletion/reduction vs. continuous expression in human tumor cells as correlated with their malignancy. Int J Cancer 1998;76:284-9.
8) Aminian A, Mirsharifi R, Alibakshi A, Khorgam Z, Dashti H, Hasani SM. Relationship between Esophageal Cancer and Blood Groups. World Appl Sci J 2010;8:503-8.
9) Jovanovic-Cupic S, Stamenkovic G, Blagojevic J, et al ABO histo-blood groups and RH systems in relation to malignant tumors of the digestive tract in Bosnia and Herzegovina. Arch Biol Sci Belgrade, 2008; 60, 593-99.
10) Beckman L, Angqvist KA. On the mechanism behind the association between ABO blood group and gastric carcinomas. Hum Hered 1987;37:140-43.
11) Kurtenkov O, Klaamas K, Miljukhina L. The cancer level of natural anti- Thomsen-Friedenriech antigen (TFA) agglutinins in sera of patients with gastric cancer relaed to ABO (H) blood phenotype. International Journal of Cancer. 1995;60:781-785.
12) Henderson J, Seagrott V, Gold Acre M. Ovarian cancer and ABO blood groups. J Epidemiol Community Health 1993;47:287-9.
13) Auclair CL. Altered H-antigen reactivity as an early indicator of malignant transformation in oral epithelium. J Oral Pathol 1984;13:401-11.
14) Dabelsten E, Pindborg JJ. Loss of epithelial blood group substance in oral carcinoma. Acta Path Microbial Scand 1973; 81: 435-44.
15) Ramesh G, Pathak S, Gupta B, Raj A, Pathak R. Is Blood group an important factor in oral cancer?–A Review. Rama Univ J Dent Sci. 2015;2(4):17-22.
16) Bhateja S, Arora G. ABO blood groups and oral premalignancies: A clinical study in selected Indian population. Indian J Cancer 2014;51:219-21
17) Sharma G, Choudhary R, Bharti D. Studies showing the relationship between abo blood groups and major types of cancers. Asian J Exp Sci 2007;21(1):129-32.
18) Jaleel BF, Nagarajappa R. Relationship between ABO blood groups and oral cancer. Indian J Dent Res 2012;23(1):7-10.
19) Xie J, Qureshi AA, Li Y, Han J (2010) ABO blood group and incidence of skin cancer. PLoS One, 5, 11972; 11-12.
20) Biondi C, Campi C, Escovich L, Borras SG, Racca A, Cotorruelo C. Loss of A, B and H antigens in oral cancer. Inmunologia 2008;27(3):127-31.
21) Toto PD, Nadimi H. Co-expression of cytokeratins, involucrin and blood group antigens in oral squamous cell carcinoma. Oral Surg Oral Med Oral Pathol 1990:70:75-80.
22) 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(3):1415-8.
23) Gopal Reddy VK, Moon NJ, Sharva V, Guruprasad, Reddy EK, Chandralkala S. Is there an association between oral submucous fibrosis and ABO blood grouping? J Cancer Res Ther 2016;12(1):126-30.
24) Saxena S, Gupta KK, Meena P. Association of ABO Blood Groups in Relation to Oral Cavity Cancers in Western Rajasthan. Int J Contemp Med Res 2016;3(9):2661-4.