A RETROSPECTIVE STUDY OF BLOOD GROUPS IN HEAD AND NECK MALIGNANCIES

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ABSTRACT

BACKGROUND
Malignancy is a unique disease with abnormal proliferation of cells with the properties of invasion, anaplasia and metastasis. It accounts for around 12% of the deaths throughout the world. Blood does vital tasks around the clock. Blood is a mysterious fascination for man since the dawn of time. Malignancy has a multifactorial aetiology, in which genetic factors also have an influence.

Aim- To study the risk of various Head & Neck malignancies among different blood groups.

MATERIALS AND METHODS
This is a retrospective study done at Vijayanagara Institute of Medical sciences Ballary, Karnataka; in proven cases of head and neck malignancies from June 2015 to December 2016.

RESULTS
The susceptibility of head and neck malignancies is found to be highest among the individuals of B, A, O, AB blood group with Rh antigen positivity, in descending order and least susceptibility was found among O negative individuals.

CONCLUSION
From this correlation study of blood groups and Head and Neck malignancies, it follows that there is an inherited element in the susceptibility of Head and Neck cancers among different blood groups.

KEYWORDS
ABO Blood Group, Rh System, Head and Neck Malignancies, Chromosome.

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BACKGROUND
Malignancy is a unique disease with abnormal proliferation of cells with the properties of invasion, anaplasia and metastasis. It accounts for around 12% of the deaths throughout the world. About 57.5% of global head and neck malignancies occur in Asia especially in India for both sexes. Malignancy has a multifactorial aetiology, in which genetic factor also have an influence. And the current thinking on the origin of malignancy is that it is a phenotypic manifestation of accumulative genetic changes in normal cell.

In India, malignancy has been one of the leading cause of deaths, nearly 1.5-2 million malignancy cases at any point of time. In India, majority of head and neck malignancies present with a stage 3 or 4 disease. While most of the efforts usually focus on therapy and outcomes, the need for risk factors evaluation, screening for early detection cannot be overlooked.

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The A, B, O blood group systems were first described by Karl Landsteiner in 1900 and the AB blood group was later described by Von Decastallo and Sturli in 1902.

The ABO blood group system comprises 4 blood groups: O, A, B and AB. Patients of all groups have a common H antigen on the red cell membrane surface, which is coded for by the H gene on chromosome 19. This H antigen may then be acted upon by further enzymes, depending on the presence of ABO genes on chromosome 9.

The Rh system (originally termed ‘Rhesus’ system, when discovered in Rhesus monkeys) is a complex system of 45 antigens encoded on chromosome 1.

Blood group antigens, which are the alloantigens in humans, are present on the surface of red blood cells and epithelial cells. In Malignancies derived from epithelial cells, genetic factors coding for each blood antigens have influence on oncogenesis.

The possibility of association between ABO blood groups and malignancy was first explored by Anderson D E and Hass C. Since then many studies have reported the high incidence of blood group A in various malignancies including neurologic tumours, salivary gland, colon, uterus, ovary, pancreas, kidney, bladder and cervix and likewise O blood group in skin malignancy like melanoma.

MATERIALS AND METHODS
This was retrospective study conducted in Vijayanagara Institute of Medical Sciences, Bellary, Karnataka, from June 2015 to December 2016.
In this study, (table 2) most of the cases presented with the most debatable neck node entity N0. In this aspect also, there was no significant difference in the ABO system, Rh type and the neck node status.

In this study (Chart 3) most cases of Rh positive type had been diagnosed with stage 3 and 4 disease at the time of presentation, meanwhile Rh-negative type were diagnosed with stage 1 and 2 disease. Hence inferring that Rh-positive type blood group has rapid growth and invasive property than Rh negative blood groups. And also the recurrence rates (patients with recurrent malignancy) were high among the Rh positive blood groups in the follows descending order (B+ve, A+ve, AB+ve, O+ve) than the Rh negative blood groups (p value <0.001 - highly significant).

In our study we have found that B+ve and A+ve blood group individuals with risk factors (almost 65% of the above-mentioned blood group types) and without risk factors (33%) have developed head and neck malignancy over a period of time. Whereas in other blood group types like O+ve, AB+ve, O-ve, B-ve, A-ve about 80-100% of individuals were having risk factors like smoking, alcoholism, beetle nut/tobacco chewing etc.

Hence compared to other blood groups, B+ve and A+ve blood groups are at risk of developing Head and Neck malignancies even without exposure to the risk habits. Whereas in other blood groups the genetic alteration in the cells is explained with the exposure to risk factors.

And also the duration of exposure to these risk habits were longer (averages to 45 years) in case of B-ve blood group, whereas for in all other blood group types, the duration of exposure to the risk habits were less (averaging to 25 years). So concluding that even though B-ve blood group is more prone for developing malignancy, there has to be a long term exposure to other risk factors.

### Table 1. Blood Group Distribution in Relation to Each Site of Head and Neck Malignancy

<table>
<thead>
<tr>
<th>B+ve</th>
<th>A+ve</th>
<th>O+ve</th>
<th>AB+ve</th>
<th>A-ve</th>
<th>B-ve</th>
<th>O-ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>13</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Larynx</td>
<td>15</td>
<td>7</td>
<td>9</td>
<td>4</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Thyroid</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cervical lymph node</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PNS</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>P&lt;0.000, Highly Significant</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Blood Groups and Neck Node Status

<table>
<thead>
<tr>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>B+ve</td>
<td>16</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>A+ve</td>
<td>12</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>O+ve</td>
<td>12</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>AB+ve</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>B-ve</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>A-ve</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>O-ve</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
DISCUSSION

Human genetics is much beyond the mere hereditary disorders. Genetic studies have emerged a lot even to a level to understand how these endogenous factors influence the development of disease, and also how it interacts with other factors.

In our Indian population the distribution of ABO blood group is as following the most prevalent being blood group O followed by B, A, AB blood group.  

ABO blood group system is mapped at 9q34.2 region, the genetic alteration of this loci is seen in many cancers. These loci, code for blood group antigens which are surface antigens of red cells and epithelial cells. Hence any genetic alteration will cause the genetic change of epithelial cells and it increases cellular motility or facilitate the interaction between tumour cells and endothelial cells of distant organs.  

The precursor antigen for the formation of A, B, AB blood group is H antigen. All groups have a common H antigen on the red cell membrane surface, which is coded for by the H gene on chromosome 19. This H antigen may then be acted upon by further enzymes, depending on the presence of ABO genes on chromosome 9. Each person inherits two ABO genes. The O gene is nonfunctional so that if an individual has not inherited either the A or B gene, then the H antigen alone is detected on the red cell surface. Such individuals are Group O. However, if an individual has inherited an A or B gene then each code for a specific enzyme which adds a specific sugar to the H gene product producing either the A, B or AB phenotype.

Individuals having O blood group have the highest amount of H antigen, which offers protection against oral cancers. This ABH antigens on the epithelial cells are carbohydrate antigens which regulates the pattern of epithelial differentiation and the cell maturation.  

Our study has showed that Blood Group B is associated with laryngeal and hypopharyngeal malignancy. This finding is in agreement with Khushboo Singh et al who has reported that laryngeal cancers are found more in blood group B. But in another study by Adam SI et al, also showed that laryngeal malignancies are more seen in blood group A.  

From this study we have analysed that Blood Group A is more prone for oral malignancies. The other studies by Jaleel B et al has also showed a similar result, that blood group A has the highest potential of developing oral malignancies. In another study by Chordia et al has demonstrated that people with A blood group are 3.98 times at greater risk to develop oral malignancies.  

Individuals with blood group A express A –like antigen (Forssmann or Tn antigen). This antigen was detected in malignant cells. Malignant cells are capable of a antigen expression even in individuals with blood group B and O. Thus, antibodies to A attack precancerous and cancerous cells expressing this antigen. Individuals with A and AB blood groups lack these antibodies hence they are more likely to develop oral malignancies.

These blood group antigens are also present on epithelial cells of various tissue. Malignancies are associated with down regulation of glycosyl transferase that is involved in the biosynthesis of A of A and B antigens. Partial or complete deletion of these antigen due to genetic alteration of its synthesis results in cell surface changes. This alteration of the antigen pattern on cell surface is associated with tumorogenesis.  

In our study 2 cases of salivary gland malignancies, of which both were blood group A which is similar to other studies in which blood group A were susceptible for salivary gland malignancies.  

In this study we have found that there is no significant difference in different ABO system and the neck node status and the degree of differentiation of the squamous cell carcinoma.
The Rh gene is located on the short arm of chromosome 1 where some oncogenes are also located, but the linkage analysis is still not clear.

In another study by Hamed et al and others they have found that there is no relationship between Rh factor and developing oral malignancies. In other studies (Pinkston and Cole, De Manzoni et al) they also didn’t find any relationship between Rh factor and human carcinogenesis.

However, in this study we have found that Rh positive blood groups have a rapid growth pattern and invasiveness property and also high recurrence rates than the Rh negative blood groups.

But, Jovanovic Cupic et al has concluded that Rh negative had high proportion of digestive tract malignancies. Bryne et al suggested that the five-year survival rates in Rh positive malignancy patients were considerably better than those Rh-negative patients.

The effect of Rh system in pathological process may be related to the physiological role of complex proteins of Rh system in the transport of toxic biological gases such as ammonia or carbon dioxide to detoxifying organs e.g. liver and kidney. Hence association between Rh system and malignancy might be related to linkage disequilibrium.

Hence, patients clinically suspected of head and neck malignancies with or without risk factors should always be screened for blood group/Rh typing which is cheap and highly cost effective, since there is a statistically significant correlation between ABO/Rh typing and Head and neck malignancies.

These at risk blood group patients with premalignant lesions and conditions should be followed up regularly and should be counselled.

Limitation of the Study
A large series studies is needed to elucidate and confirm the association between blood groups and head and neck malignancies.

CONCLUSION
Patients clinically suspected of head and neck malignancies with or without risk factors should always be screened for blood group/Rh typing which is cheap and highly cost effective, since there is a statistically significant correlation between ABO/Rh typing and Head and neck malignancies.

The time duration of exposure to the risk factors for the development of Head and Neck malignancies appears to influence the genetic alteration frequently in non-at-risk blood groups.

These at risk blood group patients with premalignant lesions and conditions should be followed up regularly and should be counselled.

In the future the evaluation in clinically suspected head and neck malignancies should include the genome study of chromosomes determining blood group and Rh type.

The future of the study is the gene tailoring and gene therapy should be focussed more on at risk blood groups with or without risk factors.

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REFERENCES


