

Association of ABO blood groups in relation to gastrointestinal cancers in Jodhpur

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Abstract: Previous studies supported a link between the ABO blood type and survival for several types of malignancies. Nonetheless, the relationship between ABO blood type and gastrointestinal cancers has not been rigorously evaluated. However, in relation to GIT cancers, these findings are inconsistent and contradictory. The goal of this retrospective analysis study was conducted for analysis to access ABO blood groups potential role of in GIT carcinoma. The study was conducted in the Department of Physiology in collaboration with the Department of Radiotherapy at Mathura Das Mathur Hospital of Dr. S. N. Medical College, Jodhpur (Rajasthan), on 174 clinically diagnosed GIT cancer patients out of which 76 were males and 98 were females. The study period was from September 2006 to March 2008. The standard agglutination test was used to determine the blood groups. The statistical association of ABO blood groups and risk of gastrointestinal tract cancers was found out with Odd Ratios (OR). Maximum GIT cancer cases (66 out of 174) were found in blood group A individuals (Odd Ratios {OR}-8.25) in reference with blood group AB (cases-12; OR- 1). Thus it is reported that blood type A highly associated with GIT cancers, followed by B, O and AB type. The female were found to be higher incidence to develop of GIT cancer in comparison to males.

Keywords: Blood type and rectum cancers; Cancers; esophageal cancer; GIT cancers; pancreatic cancer and ABO blood type

INTRODUCTION

The ABO blood type, an easily accessible factor in patient's genetic makeup, has been associated with many diseases, though the explanation for the association between ABO blood groups and some disease is still unclear. Since the first report showing an association between blood group A and gastric cancer [1], numerous other reports have also documented a relation between susceptibility to cancer and blood group.

ABO blood group has been associated with risk and survival of several malignancies, including pancreas cancer [2], stomach cancer [1]. The mechanism is complex and unclear. Blood group antigens may influence the systemic inflammatory response [3] that has been associated with the malignancies. Blood group antigens are expressed in many other tissues, including breast ductal cells, lobular cells and even some malignant cells [4]. The ABO antigen expressed on the surface of malignant cells appears to be different from the antigen expressed on normal tissue [5]. These

mechanisms might influence the initiation and spread of malignancies.

High incidence of blood group A in various cancers, including neurologic tumors, salivary gland, colon, uterus, ovary, pancreas, kidney, bladder and cervix [6] and consistent relation to O blood group in skin and melanoma has been reported [7].

The mechanisms hypothesized behind the association between blood group A and gastric carcinoma is that the carcinoma cells produce an antigen immunologically related to blood group A which particularly in O individuals may have a protective effect by preventing the growth and spread of the tumor. Because of this similarity, antibodies to A probably also attack precancerous and cancerous cells expressing this antigen. The homotypic and heterotypic cell adhesion mediated by interactions of certain blood group carbohydrates with corresponding lectins is a critically important event at the extravasations' step of the metastatic cascade when metastatic cancer cells

escape from circulation into distant sites of secondary tumor growth. People with blood groups A and AB lack antibodies to A and so are more prone to develop these carcinomas. The authors also propose that there is a small association between blood type A and cancer development. Type A individuals appear to be at a moderately increased risk for many cancers. Deletion or reduction of histo-blood group A or B antigen in tumors of A or B individuals is correlated with the degree of malignancy and metastatic potential in many types of human cancers [6].

ABO blood group genes are mapped at 9q34.2 region in which genetic alteration is common in many cancers. Thus, blood group antigen expression may be affected by genetic change of tumor. A correlation of blood group antigen expression in tumor with metastasis and prognosis has been reported for various human malignancies, such as, colon, breast and prostate cancer as the blood group carbohydrates expressed on cell surface of metastatic cancer cells function as cell adhesion molecules. The loss or presence of blood group antigens can increase cellular motility or facilitate the interaction between tumor cells and endothelial cells of distant organs [8].

In many cancers, the deficiency of A or B epitope has been reported which is associated with accumulation of their precursor, which causes enhanced malignancy, though the molecular genetics mechanism leading to such phenotypic changes is not known. The expression of certain blood group carbohydrate antigens on the surface of cancer cells thus can be regarded as an end product of tumor progression that can be used as useful prognostic and diagnostic purposes [9].

The present study is an attempt to correlate ABO blood groups frequency and to assess the utility of ABO blood group in relation to GIT cancers as a preclinical tumor marker. Thus, the objectives of this study were to document ABO blood group of patients suffering from malignancies of GIT and to describe the association of malignancy with ABO blood group in Jodhpur in Western Rajasthan.

MATERIAL AND METHOD

This was a retrospective hospital based study, conducted in the Department of Physiology in collaboration with the Department of Radiotherapy at in Mathura Das Mathur Hospital in Jodhpur, Rajasthan from September 2006 to March 2008. A total of 174 consecutive, newly and confirmed diagnosed GIT cancer patients were enrolled in this study as patient group. The study was approved by Ethical Committee of Dr. Sampurnanand Medical College, Jodhpur under Rajasthan University of Health Science, Jaipur.

A written informed conscious consent was obtained from all subjects before their participation.

The data of age, sex, ABO blood group and pathological status of cancer were collected from the Radiotherapy Department of Mathura Das Mathur Hospital, Jodhpur.

Inclusion criteria for the cases were as follows

Pathologically confirmed diagnosis of GIT cancer, Laboratory data available for ABO blood type and detailed record of disease, course and history

Exclusion criteria

Familial cancer history, dietary habits, drinking alcohol had been taken.

METHODOLOGY

Initially all patients completed a detailed questionnaire regarding their diet and habits, submitted to thorough history taking, detailed physical examinations and performed routine radiological and laboratory investigations including complete blood count (CBC) and tumor markers for GIT cancer. Blood samples were obtained via vacuum glass tubes containing EDTA.

ABO blood typing was carried out with standard agglutination method. ABO blood groups were determined by using antiserum A and Antiserum B [10].

Standard Agglutination Method

In agglutination test firstly we prepare red cell suspension in a test tube and then in under aseptic precautions add a drop of blood. Then a drop of each antiserum (antiserum A, antiserum B) on is placed on glass slide with the help of dropper and a drop of isotonic saline (used as control) also placed on the slide. The slide is accordingly labeled as anti- A, anti- B and control. After 10 minutes, examined for the presence of agglutination (clumping of RBC) under low power microscope, if there is no agglutination (RBC remain separated and evenly distributed), and if agglutination occurs the RBC are massed together in clumps.

Sample size determination

The sample size was determined by using the formula for comparing the difference of means between the groups with $\alpha = 0.05$, power = 80% and es = 0.3 [11].

es = largest difference between any two groups to be detected / expected within the group Standard Deviation

$$es = \text{diff} / SD$$

Sample size = 174

Accordingly we found that the sample size of 174 of GIT cancer patients would be more useful for our study purpose.

STATISTICAL ANALYSIS

For each factor, we calculated the adjusted Odds Ratios (OR) using maximum likelihood estimation.

RESULTS

Table-1: Distribution of cancer cases in relation to different GIT cancers.

S. No	Cancerous organ	No of cases	Percentage
1	Oesophagus	57	32.75
2	Colon	49	28.16
3	Rectum	23	13.21
4	Pharynx	14	8.04
5	Gall bladder	13	7.47
6	Liver	07	4.02
7	Anus	06	3.44
8	Caecum	05	2.87

Table-1 shows that in distribution of all diagnosed 174 gastrointestinal cancers the maximum cases of esophageal and colon cancers (32.75% &

28.16% respectively) were found and least cancers cases were related to anal and caecum cancers (3.44% and 2.87% respectively).

Table-2: Distribution of percentage of Gastrointestinal Tract cancers (Gender Wise)

	No of patients	Percentage
Male	76	43.68
Female	98	56.32

Table-2 shows that in gender wise distribution of gastrointestinal cancers the number of female cancer

patients having the largest percentage (56.32 %) in comparison with male (43.68 %).

Table-3: Association of Gastrointestinal Malignancy with ABO Blood Groups

S. No	Type of GIT Malignancy	No. Of Cases	Cases in Blood Groups							
			A		B		O		AB	
			No	*OR	No	*OR	No	*OR	No	*OR
1	Esophagus	57	21	7.79	10	2.82	22	8.33	4	1 (R) **
2	Colon	49	19	9.71	16	7.43	11	4.44	3	1 (R) **
3	Rectum	23	06	2.35	09	4.29	05	1.85	3	1 (R) **
4	Pharynx	14	06	9.75	03	3.55	04	5.2	1	1 (R) **
5	Gall bladder	13	06	10.29	05	7.5	02	1 (R) **	-	-
6	Liver	07	03	4.5	02	2.4	01	1	1	1 (R) **
7	Anal	06	03	1	03	1 (R) **	-	-	-	-
8	Caecum	05	02	2.67	02	2.67	01	1 (R) **	-	-
	Total	174	66	8.25	50	5.44	46	4.85	12	1 (R) **

*OR=ODD's Ratio **(R) =Reference OR

Table 3 shows the association of ABO blood groups with different types of gastrointestinal cancers. In overall cancer cases (174) maximum gastrointestinal cancers was found in patients having blood group A (OR 8.25) in reference to blood group AB. In reference to blood group AB (1), blood group A (OR 8.25) having highest association with gastrointestinal cancers, followed by blood group B (OR 5.44), O (OR 4.85).

The present study concluded that maximum number of GIT cancers were associated with blood type A patients and least were with blood group AB. The female were found to be higher incidence to develop of GIT cancer in comparison to males.

The association of blood group A is an interesting one in view of the suggestion of earlier immunologist that the heightened surveillance and overactive immune activity tend to result in less malignancy, whereas overly tolerant immune activity

DISCUSSION

tends to encourage it. These observations suggest that a more general hypothesis that in the tissues of all people, both normal and cancerous, there are A- like antigens present on the biochemical level that are usually inaccessible to the immune system. However, when stimulated by an autoimmune process, or the immune response to a growing cancer, the antigen becomes accessible. At that point, blood group A person, who cannot make anti-A antibodies will be more likely to tolerate cancer, and blood group A person's immune system will be less likely to attack the body's own tissues [12].

The present study reported that blood group A have the highest association of GIT cancer in population of Jodhpur. Blood group AB had found the least association with breast cancer. Blood type B and O also have some association with GIT cancers but slightly less than blood type A.

In the last 25 years, there has been a tremendous amount of work published on the chemistry of blood group antigens and tumor immunology. As cells (e.g. in tissue) become malignant, they tend to lose normal antigens and acquire new antigens; these are so called tumor antigens. It has been proven that ABO antigens diminish on malignant cells as the malignancy progresses; the loss of A, B and H antigen is proportional to the metastatic potential of the tumors [13, 14].

The reason that deletion or reduction of the A or AB antigens in tumors of A or B individuals correlate with malignancy and metastatic potential may be due to lack of adhesiveness that a cancer cell achieves when it loses blood group antigens. The loss of blood antigens result in the tumor cells gaining the ability to move and circulate through the body, because blood type antigens loss the ability to express many of cell adhesion proteins, such as integrins, which normally express an A like antigen on their receptor and control cell movement [15].

Many malignant cells (such as those found in breast and stomach cancer) develop a tumor marker called Thomsen- Friedenreich (T) antigen, which is suppressed in normal healthy cells. Tn antigen (precursor of T antigen) only becomes unsuppressed as a cell become malignant. T and Tn antigens show some structural similarity to A antigen [16]. Blood group A individuals have the least aggressive antibody immune response against the T and Tn antigens and they are actually immunologically considered similar because of their shared terminal sugar (N- acetyl-galactosamine), and so might be readily confused by immune system of blood group A individuals. Blood group A cancer patients had the greatest and most uniform suppression of the level of Tn antigens, irrespective of age, cancer

stage, or tumor morphology and lower level of anti-B isohemagglutinins. This is probably at least a part of the explanation for the poorer outcomes in many cancers among blood group A individuals [17].

Hakomori suggested that if the immune surveillance theory is correct and we recognize tumor antigens as foreign, leading to attack of the tumor, then the "A-like" properties of tumor antigens may not be recognized by group A patients [18]. Tumor Immune Surveillance in the immune system can specifically identify and eliminate tumor cells on the basis of their expression of tumor specific antigens or molecules induced by cellular stress whereby immune system identifies the cancerous or precancerous cells and eliminates them before they can cause harm [19].

In another study by Bennett Malisa [20], found that blood group A exhibits increased levels of P-glycoprotein which may indicate why individuals may not respond to conventional chemotherapy as well as other blood groups. It would be interesting to know that the percentage of patients in this particular study were of Blood Group "A". It appears that a more integrated treatment protocol should be considered using conventional modalities as well as dietary modifications. Blood Group "A" individuals have a very low immunologic response to T and Tn antigens because they share the same sugar (N-acetylgalactosamine). This allows the cancer cells to bypass the immune system and replicate with little interference from the type A antibodies. Breast cancer in general can be very invasive depending on how well-differentiated the cancer cells appear. The more differentiated a cancer cell becomes; the greater its ability to adhere to other cells. A blood group "A" individual with a breast cancer diagnosis must primarily focus on creating a nutritional strategy which will have an effect on cancer survivorship.

It has been consistently observed that blood type A is associated with an increased risk for stomach cancer and poorer survival. Some researchers have hypothesized gastric cells produce an antigen immunologically related to blood group A known as A-like Thomsen- Friedenreich (T) antigen. Blood type individuals, have a tendency to a lower natural Anti-Thomsen-Friedenreich immune response. The presence of p53 mutations is associated with stomach cancer and with blood type a [21].

In a study, the increased number of pancreatic cancer was found among the patients with blood group B and a decreased number in patients with blood group O as compared to control have been reported [22]. Another study suggested the positive association with a blood group in pancreatic cancer and slight association

with a in liver cancer and in gall bladder and bile duct cancers strong associations with A and B [23].

According to Henderson *et al.*, [6], people with blood groups A and AB lack antibodies to A and so are more prone to develop these carcinomas. In another study of colon cancer, a weak association with a group and an altered blood group antigen expression related to progression of malignancy, had been reported [24]. Hakomori [18], demonstrate that A and B phenotypes aberrantly expressed in various types of human cancer, and their genetic basis, have been studied. They widely observed in a large variety of human cancers is deletion of A or B epitope, assimilation of their precursor H {Le(y), Le (b)}, which causes enhanced malignancy.

Limitations: Because of resource constrain, small sample size and short time duration for the present study, the another view that the identification of genetic and environmental factors among racial and ethnic groups should offer some insights into the observed epidemiological data and advance opportunities to better understand the control and development of cancer. Collectively, we could hypothesize that tumors have more chance to thrive and maximum found in blood group a patients than those in other blood group

CONCLUSION

In conclusion, it appears that different blood groups are associated with different manifestations of the disease. Blood group A apparently increases the risk for cancer. Different GIT cancers have the strongest association with blood type A group. But the racial and ethnic distribution of blood groups and size of sample is an important factor for predicting the cancer risk. Blood type needs to be considered together with other risk factors to understand the individual patient's risk. The identification of genetic and environmental factors among racial and ethnic groups should offer some insights into the observed epidemiological data and advance opportunities to better understand the control and development of cancer.

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