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Exploring the relation between ABO blood group and cancer prevalence: A comprehensive review

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Abstract

Blood group and cancer prevalence shown to have certain correlation in them. The findings from various studies, examining the correlation between ABO blood group types and the risk of specific cancers such as breast, colorectal, lung, head and neck, gastric, and ovarian cancers. Review reports, when blood types A, B, AB, and O are compared to one another, blood type O is more common in many cancer instances, whereas blood types A, B, and AB are more common in only a few cancer types. Blood group AB has a much-decreased risk overall. Current review reflects the findings of different researches and compr

ehend the findings to build better vision of the concept which will build pioneer path to led the concept in futuristic way. Current review will also help in developing strategies for risk management of cancer.

Introduction

The word "blood group" refers to a system of red blood cell (RBC) antigens, each of whose properties is governed by a set of genes. These genes may be allelic or located close to one another on the same chromosome.[1] However, when tested with antisera inside a specific system, "Blood type" refers to a specific reaction pattern. Important blood groups including O, A, and B were found using logical and compelling scientific reasoning, as well as compatibility testing and transfusion protocols. Karl Landsteiner received the Nobel Prize in 1930 as a reward for this accomplishment.[2] The ABO blood group type is the most significant factor in medicine.[3] The presence or lack of antigens on the surface of red blood cells determines the ABO type classification.[4,5] Phenotypes with different and genetically generated glycoconjugate structures are displayed by the ABO blood type antigen. Numerous illnesses, including diabetes and cancer, are brought on by a lack of antigens. A significant risk of cancer arises from the presence or lack of antigens on the surface of red blood cells.

The research of many diseases greatly benefits from the use of the ABO blood group classification. There

are disagreements over the relationship between ABO blood types and vulnerability to particular infectious and non-infectious diseases, such as cancer, diabetes, cardiovascular disease, malaria, hematologic disorders, etc., because some blood groups lack antigens.[6,7] The absence or presence of antigens on the surface of RBC causes a major risk of cancer. Blood types can induce changes in the structure and function of blood membranes due to the presence or absence of antigens. The functions linked to blood type structures can be correlated with both diseases and overall health.[8]

Erythrocytes, also known as red blood cells, are a vital part of the human body. They help transport gases and nutrients throughout the body. They are able to perform this essential job because of their distinct composition and structure. Erythrocytes play a key role in the research of numerous disease processes in diverse body systems. These specialized cells must carry oxygen from the lungs to tissues for metabolic functions including ATP generation during their roughly 120-day lifespan. Additionally, they collect carbon dioxide generated in the periphery and transport it back to the lungs for elimination. When erythrocytes reach the lungs, they contain hemoglobin with ferrous heme (Fe), which has a strong affinity for oxygen.[9]

Blood group antigens are present on white blood cells, specific tissues, plasma proteins, platelets, and diverse cell surfaces. Additionally, they can be found in bodily fluids like sweat, saliva, breast milk, seminal fluid, urine, gastric secretions, and amniotic fluid in a soluble form.[10] Gene expression patterns can alter as cells develop cancer.[11] In order to cause cancer, scientists believe that environmental changes impair cells' capacity to signal and communicate with one another as well as the immune system's capacity to recognize typical conditions for cell growth. In 1901, Landsteiner's discovery prompted the study of the ABO blood group system as an etiological factor for numerous diseases, such as stomach carcinoma and peptic ulcers.

One of the biggest differences between normal and cancer cells is that normal cells only grow when they get a certain number of signals. Cancer cells can grow even when they don't get any signals, which is one of the many ways that they differ from normal cells. Cancers are identified by the location of their development and the specific cell type from which they start, regardless of whether they spread to other parts of the body. Leukemia, for example, is a blood cell-derived cancer. When the body produces too many aberrant white blood cells, it disrupts the bone marrow's production of red blood cells and platelets. On the other hand, lung cancer is a type of cancer that begins in the lungs and spreads to the liver. Either the ducts or the lobules are where breast tumors start. With its six main characteristics, carcinogenesis can happen in any cell, tissue, or organ, resulting in degenerative changes and the development of various cancers. Key processes enabling this progression include avoiding apoptosis, possessing limitless proliferative potential, heightened angiogenesis, resistance to anti-growth signals, activation of self-growth signals, and the capacity for metastasis. The intricate process of carcinogenesis is predominantly initiated by environmental factors and genetic predispositions.[8]

Blood type antigens are pivotal in the processes of tumorigenesis, metastasis, and prognosis, actively engaging in cell recognition, signaling, and adhesion. Changes in the presence of ABH and associated antigens occurs throughout cellular development, aging, and differentiation, particularly evident in carcinogenesis and pathological processes. ABH antigens are present in epithelial tissues of the gastrointestinal tract, lung, breast, mouth, uterine cervix, bladder, and prostate. However, malignant tissues in these areas lack these antigens in glycolipids and glycoproteins. As malignancy advances, loss of normal antigens, and acquisition of tumor antigens occur, and the decrease in A, B, and H antigens is inversely related to the tumor's metastatic potential. Blood type antigens exhibit procoagulant and angiogenic characteristics, serving as ligands for selectins, enhancing cellular motility, and resisting apoptosis.[12] These biological functions likely contribute to tumor development, and a proposed model aims to explain the observed correlations between these markers and disease outcomes.

Relation of ABO Blood Group and Cancer Prevalence

The exploration of potential links between ABO blood groups and cancer has garnered increasing attention in recent years. This literature review aims to systematically examine existing research, incorporating a meta-analysis to provide a comprehensive overview of the relationship between ABO blood groups and various types of cancer. In 2014, a study examined the connection between the ABO blood group and cancer risk, analyzing over 100 cases. The findings revealed varying percentages of association between blood groups and different types of cancer. Notably, blood group A showed an elevated risk, while blood group O exhibited a decreased risk of developing.[13] In a prospective cohort research, Huang et al. documented the association between ABO blood type and the risk of several types of cancer. The study also looked into how the ABO blood type is inherited. The Cox proportional hazards model was used to determine the hazard ratios for both all malignancies and particular cancers.[14] According to the results, blood types B and AB were substantially linked to a decreased risk of colorectal and gastrointestinal malignancies. Furthermore, blood type AB had a significantly higher risk of liver cancer, whereas blood type B demonstrated a significantly reduced risk of stomach and bladder malignancies. When categorized by histological type, blood types B and AB were linked to lower risks of sarcoma, lymphoma, leukemia, or other cell types of cancer. This study underscores the role of genetic traits associated with ABO blood type in the development of cancers in the gastrointestinal and urinary tracts.[15]

ABO Blood Groups and Cancer Types

Breast cancer

Breast cancer is a type of cancer that starts in the breast. Several studies have explored the association between ABO blood groups and breast cancer risk. Blood groups A and O accounted for a larger proportion of the 329 patients studied in 2014 than any other blood group. Additionally, it was shown that the predictive value was higher for the A and O groups.[16] In a different study, 250 patients were examined and categorized based on their blood type. The correlation between ABO group

type and breast cancer using comparison between the patients with healthy Donor (control) and the frequency and percentage of patients was in blood group A with 64%.[17] Another study in 2014, indicates there was no significant relative frequency of breast cancer in any particular blood group and that blood group was not a significant factor for breast cancer.[18]

Colorectal cancer

Colorectal cancer of the colon or rectum, located at the digestive tract's lower end. Various studies reported the correlation of ABO blood group with colorectal with various number of patients, also study conducting this extensive study to find risk factors of the disease, particularly the role of genetic factors and disease prevention, in susceptible host. According to researcher individuals with blood type O, for instance, may exhibit an increased susceptibility to colorectal malignancies and they do not find any type of correlation between ABO blood group and colorectal Cancer. While certain studies indicate a potential link, more robust evidence is required to draw conclusive associations.[19-22]

Pancreatic cancer

Cancer that begins in the organ lying behind the lower part of the stomach (pancreas). In a study conducted by Julia *et al*. (2010)[23] involving 274 patients compared to the ABO groups of 708,842 unique blood donors to the Central Blood Bank in the Pittsburgh area over the past approximately 30 years, the authors investigated the association between ABO blood groups and pancreatic cancer.[8] Compared to the ABO distribution among regional blood donors, the results showed a statistically significant increase in the frequency of blood group A among patients with pancreatic cancer. **Table 4** shows high frequency of 42.80% in Blood Group O. Conversely, the frequency of blood group O was found to be significantly lower among pancreatic cancer patients compared to the community blood donors, that report contributes valuable insights into the potential link between ABO blood groups and pancreatic cancer susceptibility.[24]

Lung cancer

Conflicting findings are present regarding the correlation between ABO blood groups and lung cancer. They reported a weak association between blood type and the risk of lung cancer, which was not statistically significant. Their case-controlled studies suggested a higher risk of lung cancer with blood type A and a lower risk with blood type B. Although some studies suggest a potential link, more robust evidence is needed to establish conclusive associations.[25] Gungor Utkan and associates (2012) examined the possible association between ABO blood type and lung cancer (LC) risk in a multicenter, case-control, observational analysis. All patients treated for lung cancer at the collaborating centres between 2000 and 2011 were included in the study. Volunteer healthy blood donors from the Turkish Red Crescent between 2004 and 2011 comprised the control group. The analysis involved 1954 lung cancer patients and 3,022,883 controls, with a notable predominance of males, constituting 84% of the patient group. The investigation explored the association of ABO/Rh with clinical features, including age at diagnosis, histological subtype, and gender. The results indicated a statistically significant association between ABO blood type and lung cancer, suggesting that having a blood type other than O increases the risk of developing lung cancer.[26]

Head and neck cancer

A group of cancers of mouth, sinuses, nose or throat. Contradictory findings exist regarding the relationship between ABO blood groups and head and neck Cancer.[27] In Head and neck cancer, containing different site from head to neck to cause cancer according to researcher's studies and according to them, on the basis of various parts or site of head neck cancer, various blood groups are found more and at all time same blood group are not found in different-different site. They cannot found exact mechanism about ABO blood group with head neck cancer.[28] We observe a trend of high frequency of Head and Neck cancer in B and AB blood group having 40% and 20% frequency respectively as shown in **Table 2** and **Table 3**.

Ovarian cancer

Gynecologic cancer is a broad category of cancers that affect the ovaries, fallopian tube, uterus, cervix, vagina, and vulva, among other female organs. Analyze the distribution of ABO and Rh blood antigen and ovarian cancer in South-East Siberia using a case-control study. It was shown that non-O blood types are linked to a 40–60% higher risk of cancer and may contribute to the development of ovarian cancer.[7]

Cervix cancer

In 2020, Hemali and his colleague conducted a retrospective study on 147 female patients in Gujarat, India, regarding ABO blood group and cervical cancer. Patients are being divided into several age-based groups, and it has been noted that blood group A has the highest frequency and blood group AB has the lowest.[29] Angel Justiz Vaillant and his colleagues conducted a case-control research in 2013 and discovered a weak correlation between blood group O and other blood groups.[30]

Lymphoma

Ling Qin et al. examined the relationship between ABO blood group and lymphoma in 13 patients from various regions and races (African, Asian, and Caucasian). They found that blood group A in Caucasian patients and O in African patients had higher rates of lymphoma and AB and B in Asian patients, respectively.[31] Researchers conducted a triple-center study in 2017 to assess the predictive value of ABO blood type in T-cell lymphoma patients. In patients with T-cell lymphoma, they provide primary treatment methods and found that ABO blood type (O vs. non-O) is a useful predictor of treatment response and an independent prognostic indicator of progression-free survival and overall survival.[32]

Skin Cancer

ABO blood group and skin cancer were investigated in 2005 by contrasting cancer patients with controls. Following the trial, it was shown that patients with blood group A had greater levels while those with blood group O had lower levels than the control.[33]

Gastric Cancer

Gastric cancer is also called as stomach cancer. It starts in the cells lining the stomach. They initially created a risk prediction model for gastric cancer based on ABO blood types and subsequently investigated the correlation between ABO blood groups and gastric cancer. Their findings revealed a higher incidence among individuals with blood type A and a lower frequency among those with blood type AB.[34] The 2012

study examined the relationship between 1045 participants' ABO blood system and their risk of Helicobacter pylori infection or stomach cancer. To find a link between ABO blood type and cancer, they carried out a meta-analysis and a case-controlled research.[27,33] The findings revealed that individuals with blood group A had a significantly higher risk of gastric cancer compared to those in the non-A groups (O, B, and AB).[36] Our research analysis shows 43.75% of frequency, best represented in **Table 1.**

Table 1: Association of blood Group A with various types of cancer

Blood Group A										
Studies	**Breast Cancer**	**Colorectal Cancer**	**Lymphoma**	**Lung cancer**	**Skin cancer**	**Cervix cancer**	**Gastric Cancer**	**Pancreatic cancer**	**Ovary cancer**	**Head Neck Cancer**
Mean	1431.789	4512.2222	395	355.625	11697.66667	51.4	367.1428571	5649.714286	2296.333333	1017.666666
Median	108	411	195	265.5	196	47	311	131	154	39
Standard deviation	5492.348603	12464.37839	48.0853	359.5794915	20052.38301	38.9011568	429.7182137	14559.58082	3722.761117	2885.953828
Variance	30165893.14	155360728.7	248089	129297.4107	402098064.3	15133	184571.8095	211981393.6	13858950.33	8328729.5
Frequency (%)	36.16%	35.99%	30.39%	40.00%	36.52%	29.01%	43.75%	36.19%	13.78%	43.41%

Table 2: Association of blood group b with various types of cancer

Blood group B										
Studies	**Breast Cancer**	**Colorectal Cancer**	**Lymphoma**	**Lung cancer**	**Skin cancer**	**Cervix cancer**	**Gastric Cancer**	**Pancreatic cancer**	**Ovary cancer**	**Head Neck Cancer**
Mean	540.1578947	1704.1111	312	166.875	4147.666667	57.6	120.2857143	2055.957143	2296.333333	433.1111111
Median	39	225	188	81.5	89	40	84	38	154	53
Standard deviation	2084.629977	4553.556068	348.9355	174.1644851	7093.999248	55.464403	96.6845632	5333.949207	3722.761117	1111.131343
Variance	4345682.14	20734872.86	121756	30333.26786	50324825.33	3076.3	9347.904762	28451014.14	13858950.33	123461.861

Frequency (%)	13.64 %	13.59 %	24.01 %	18.77 %	12.95%	32.51 %	14.33%	13.17%	13.78 %	40.00%

Table 3: Association of blood group ab with various types of cancer

Blood Group AB										
Studies	**Breast Cancer**	**Colorectal Cancer**	**Lymphoma**	**Lung cancer**	**Skin cancer**	**Cervix cancer**	**Gastric Cancer**	**Pancreatic cancer**	**Ovary cancer**	**Head Neck Cancer**
Mean	326.6842105	972.6666667	92.66	63	2483.333333	24	47.28571429	1223.571429	1314.333333	113.3333333
Median	15	76	59	23	70	10	22	17	57	6
Standard deviation	1220.596259	2725.465878	109.4547	70.58733193	4233.823016	33.91164992	37.16501171	3192.737741	2209.015467	303.2214537
Variance	1489855.225	7428164.25	11980.333	4982.571429	17925257.33	1150	1381.238095	10193574.29	4879749.333	91943.25
Frequency (%)	8.25%	7.76%	7.13 %	7.09%	7.75%	13.54%	5.64%	7.84%	7.89%	20.00%

Table 4: Association of blood group o with various types of cancer

Blood group O										
Studies	**Breast Cancer**	**Colorectal Cancer**	**Lymphoma**	**Lung cancer**	**Skin cancer**	**Cervix cancer**	**Gastric Cancer**	**Pancreatic cancer**	**Ovary cancer**	**Head Neck Cancer**
Mean	1661.263158	5349.777778	500.66	303.625	13699	44.2	304.4285714	6681	7112.333333	780.1111111
Median	57	509	255	253.5	160	40	255	88	149	28
Standard deviation	6648.78251	14900.86904	647.4537	298.438765	23562.90884	14.83913744	403.2029502	17435.15978	12171.86663	2183.771305
Variance	44206308.87	222035898.2	419196.33	89065.69643	555210673	220.2	162572.619	303984796.7	148154337.3	4768857.111
Frequency (%)	41.95%	42.61%	38.52 %	34.15 %	42.77 %	24.94%	36.28%	42.80%	42.68%	10.00%

Table 5: Mean (Average) distribution of various types cancer cases across blood groups

Studies	Breast Cancer (BC)	Cholorectal Cancer (CRC)	Lymphoma (LYM)	Lung Cancer (LC)	Skin Cancer (SC)	Cervix Cancer (CC)	Gastric Cancer (GC)	Pancreatic Cancer (PC)	Ovary Cancer (OC)	Head Neck Cancer (HNC)
Blood Group A	1431.789	4512.2222	395	355.625	11697.66667	51.4	367.143	5649.714286	2296.333333	1017.67
Blood Group B	540.157895	1704.1111	312	166.875	4147.666667	57.6	120.286	2055.957143	2296.333333	433.111
Blood Group AB	326.684211	972.6666667	92.66	63	2483.333333	24	47.2857	1223.571429	1314.333333	113.333
Blood Group O	1661.26316	5349.777778	500.66	303.625	13699	44.2	304.429	6681	7112.333333	780.111

Possible Biological Relevance

Non-O blood types may raise the chance of developing some cancers, such as pancreatic cancer, according to the ABO blood group classification. Variations in inflammation, immunological response, and the expression of molecules involved in cell adhesion and angiogenesis are some of the elements that may contribute to this link, however the biological mechanisms underlying it are still being studied. Inflammation and Immune Response, chronic inflammation is a known cause of cancer development, and ABO blood types can affect the amounts of specific inflammatory chemicals. The immune system's ability to identify and eradicate cancer cells may be impacted by ABO antigens. ABO antigens on cell surfaces have the ability to disrupt intercellular adhesion and signaling, which may have an effect on the behavior of cancer cells.[37]

Angiogenesis, or the creation of new blood vessels, is essential for tumor growth and metastasis and may be influenced by ABO antigens. These ABO-regulated chemicals contribute to cell adhesion and inflammation, which may have an impact on carcinogenesis. VWF and how it affects tumor growth and blood coagulation. Von Willebrand factor (VWF) is a blood clotting protein whose levels can be influenced by an individual's ABO blood group. Variations in VWF levels may have an impact on the development of cancer because it is also implicated in angiogenesis and apoptosis.[38-39]

ABO and processes unique to cancer, an increased risk of stomach cancer has been associated with blood type A. According to certain research, the ABO genotype may not be a major factor in the risk of prostate cancer. Compared to blood type O, non-O blood types (A, B, and AB) are linked to an increased risk of pancreatic cancer.[40] Both genomic and epigenetic factors may be involved: ABO antigens and the surrounding genetic region may be subject to epigenetic modifications, which can change gene expression and impact the development of cancer; genes on chromosome 9q34 determine the ABO blood group; and DNA sequence variations in this region may affect cancer susceptibility.[41](**Table 5**)

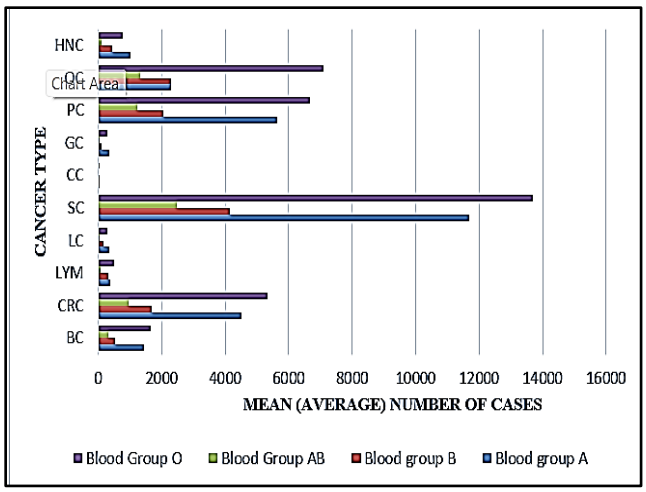

Figure 1: Mean (Average) distribution of various types cancer cases across blood groups

Conclusion

The relevance of the ABO blood group system in understanding diseases, especially cancer. The absence or presence of antigens is suggested to correlate with risks of cancer and other health conditions. Erythrocytes, or red blood cells, play a crucial role in transporting gases and nutrients throughout the body, with specific focus on their lifespan and functions related to oxygen transport. The presence of inflammatory proteins in blood, influenced by blood group antigens, is highlighted, suggesting a potential role in inflammation and related diseases. The project delves into cancer, describing its characteristics, the distinction between normal and cancer cells, and the factors contributing to carcinogenesis. Explore the correlation between the ABO blood group system and cancer is explored, with a particular focus on the six primary attributes of carcinogenesis.

After comparing blood group A, B, AB, and O with each other, blood group O show higher prevalence in many type of cancer cases while blood group A, B, and AB shows higher in only specific type of cancer. Overall, blood group AB has shown very lower risk.

The statistical results in various studies show a diverse distribution of cancer cases across different blood groups, emphasizing higher prevalence in blood group O. The frequency distribution across various cancer types indicates potential associations between blood groups and specific cancer risks. This review provides a comprehensive overview of the connection among ABO blood groups and cancer, drawing on historical context, scientific literature, and statistical analyses. The findings suggest potential associations between blood groups and specific cancer types, but the project underscores the need for further research to establish conclusive links and better understand the underlying mechanisms.

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Conflict of Interest

None.

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