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The Association between Blood Group Antigens and Gastric Cancer

[1]Nicharas Ruangprateepsaeng, [2]Nattapaweethida Rienthongkham, [2]Dharmatorn Chamroonsri, [3]Chairat Rattanasaiyai, [4]Paphada Prabhatanan, [5]Pakwan Junprateep, [5]Pavarisa Jivavitoonkit, [6]Norapatra Poobrasert, [7]Phirawat Cho, [8]Pak Boonyubol,

[1]Darunsikkhalai school (ESC), [2]Mahidol University International Demonstration School, [3]Montfort College, [4]Samsenwittayalai school, [5]Naresuan University Secondary Demonstration School, [6]The Newton Sixth Form School, [7]Assumption College Sriracha, [8]Triamudom Suksa School

***Corresponding Author:**
Nicharas Ruangprateepsaeng
Darunsikkhalai school (ESC)

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Abstract

Background: Gastric cancer is the 5th most commonly diagnosed worldwide, with the highest incidence rates occurring in Asia. Blood group antigens have been suggested as a potential risk factor for gastric cancer development, but the relationship between blood group antigens and gastric cancer remains controversial. The aim of this review is to analyse the current literature on the association between blood group antigens and gastric cancer. In addition to that, we also revised the genetic and environmental factors associated with the disease. Methods: We conducted a comprehensive search of electronic databases, MEDLINE®, Springer, ACS Publications, Google Scholar, and ScienceDirect, without temporal limitations, using English language restrictions, to identify studies investigating the relationship between blood group antigens and gastric cancer. Results: We identified previous studies that reported a significant association between ABO blood group and gastric cancer, with individuals with blood group A having a higher risk of developing gastric cancer compared to those with other blood groups. In addition to that, we identified the prognosis rate of each blood group and gastric cancer. Following with the explanation to hypotheses that may lead to gastric cancer. Conclusion: While some studies suggest a potential association between A blood group antigens and gastric cancer, more research is needed to clarify the relationship and its potential clinical implications.

Keywords: ABO blood groups, Gastric Cancer, Prognosis

Introduction

The ABO blood group system, discovered by Karl Landsteiner in 1900, serves as the most common method of classifying blood groups and is widely used in clinical practice. A single gene that encodes and alters the antigens' content in red blood cells is responsible for determining the ABO blood type. The ABO gene is autosomal, and the ABO locus is found on chromosome 9. The four major blood types are A,B,O,and AB. Blood group AB typically has the lowest prevalence, whereas blood group A typically has the greatest.

Gastric cancer refers to a variety of stomach tumours. Upwards of 95% of these tumours are epithelial in character, hence the name gastric cancer. In overall, over 1.1 million new cases and 770,000 deaths of gastric cancer were estimated in 2020. Males had a two-fold higher incidence rate than females (Ferlay *et al*, 2021). Previous research has linked reductions in gastric cancer incidence across the globe to improvements in food preservation practices as well as economic development, which leads to a decrease in the prevalence of *Helicobacter pylori* infection (Sunget *et al*, 2021). Nevertheless, it is a cancer with

a high incidence and mortality rate in some regions worldwide, including Eastern Asia. Mongolia, Japan, and the Republic of Korea had the highest global incidence, and similar patterns were observed by age group, with Eastern Asia countries having the highest incidence in both 60 and 60+ year olds (Ferlay et al, 2020). In addition, many studies indicate that there are links between ABO blood groups and gastric cancer. It is apparent that different blood groups in ABO have different gastric cancer chances. Still the association between ABO blood group and gastric cancer is a controversial topic among researchers thus we cannot surely conclude that this relationship exists.

The aim of this research was to explore the potential correlation between ABO blood groups and the risk of developing gastric cancer, as well as to analyse any possible links to clinical and pathological characteristics and patient outcomes based on online scientific literature.

Instrument

We conducted a systematic review of the scientific literature to assess the link between ABO blood group antigens and gastric cancer patients. We searched electronic databases, including MEDLINE®, Springer, ACS Publications, Google Scholar, and ScienceDirect, without temporal limitations, using English language restrictions. We used relevant keywords and Medical Subject Headings such as "ABO blood group", "gastric cancer", "relationship", "association", "survival", "prognosis", "outcome", "disease progression", and "life-expectancy". Additionally, we considered an ethnographic study that reviewed previous research from different geographic regions, including both developed and developing countries in Asia, America, Europe, and Australia. We also manually searched the reference lists of the most relevant items to identify further eligible studies not initially included in the literature search. Finally, we applied the search terms to abstracts from recent international congresses on gastric cancer.

Gastric cancer

Gastric cancer, also called stomach cancer, is a disease in which malignant cells form in the mucous membrane of the stomach. The aggressive disease of gastric cancer continues to have a debilitating effect on world health. Despite a general decline in incidence over the past few decades, gastric cancer is still the second-leading cause of cancer-related death globally and the fifth most prevalent cancer type. (Carcas, 2014). When viewed histologically, gastric cancer has significant heterogeneity at both the cytologic and architectural levels, frequently coexisting with many histologic components.(Hu, *et al*., 2012)

According to the two most commonly used classifications, which are the Lauren classification system and the WHO classification system, gastric cancer has either three main subtypes (Lauren classification) or four subtypes (WHO classification). The Lauren classification system was developed in the 1960's, and uses the structural cellular component of the disease to classify patients into three subtypes including well-differentiated, poorly-differentiated, and mixed disease. (Sexton, *et al*., 2020) Another major classification system is the 2010 WHO classification, which recognizes four main histologic patterns of gastric cancer: tubular, papillary, mucinous, and poorly cohesive (including signet ring cell carcinoma). The predominant histologic pattern of the carcinoma, which frequently coexists with less dominant features of other histologic patterns, serves as the basis for classification. (Hu, *et al*., 2012) There is another classification based on their anatomic site, gastric adenocarcinomas are largely divided into cardia (CGA) and non-cardia (NCGA) groups. The epidemiological characteristics of esophageal adenocarcinoma are shared by cancers of the gastric cardia, which develop in the vicinity of the oesophagus-gastric junction (EAC). The lower part of the stomach is where non-cardia cancer, sometimes referred to as distal stomach cancer, most frequently develops. (Rawla, & Barsouk, 2019)

Risk factor and clinical feature

There are still no clear causes of gastric cancer, but it occurs when the inner lining of the stomach gets hurt causing the DNA to mutate. This change may instruct the cell to rapidly multiply which may lead to tumour and harm nearby cells.

Genetic:

Many factors that are the result of dietary and environmental exposures are likely to affect the risk of developing cancer. The other cancer syndromes in

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families are also a risk that increase the incidence of stomach cancer.The gene most commonly associated with HDGC is called CDH1. (Cancer.Net, 2020)

Age and sex:

60 percent of gastric cancer occurs in those over 65 years old since those with higher age are more likely to have lower healing rate and vulnerable to infections. Men are twice more likely to get infected due to various factors including hormones, environment, smoking habit and more men got infected by *H. Pylori*.

Environmental factors:

Environmental factors, such as exposure to radiation or employment in the coal or rubber industries, play a significant role in modifying the risk of gastric cancer.

Geographic variation:

The development of gastric cancer is strongly influenced by nutrition, and global variations in diet probably have a significant impact. The fact that some groups with high rates of *H. pylori* infection experience an elevated risk of gastric cancer but not others with similar high rates of infection may also be explained by variations in *H. pylori* genotypes. Studies assessing the risk of gastric cancer among immigrants from high-incidence to low-incidence countries have discovered a decline in cancer risk over successive generations, further bolstering the notion that environmental factors significantly influence carcinogenesis and contribute to global variation.

Salt intake:

A significant and modifiable risk factor for stomach cancer is diet. Both the World Health Organization/Food and Agriculture Organization (WHO/FAO) expert panel and the World Cancer Research Fund/American have stated that salt is most likely a factor in the development of stomach cancer. The connection between salt and stomach cancer was initially identified by early ecological research. They discovered that those with high and moderate salt intakes had a 40%–70% higher chance of developing cancer than those with low salt intakes.

Fruit and vegetables:

Due to their high antioxidant content, fruits and vegetables may have a preventive impact against stomach cancer. However, the benefit was no longer significant when only more trustworthy prospective studies were taken into account. In fact, two similarly sized prospective trials similarly discovered little to no risk reduction with increasing fruit and vegetable consumption, despite the fact that these foods can lower blood pressure, lower the risk of heart disease, and lower the risk of stroke. (Larsson)

Blood group:

Research has shown a connection between blood group A and gastric carcinomas. Moreover, it was potentially linked to the interaction between the Lewis b blood group antigen and *H. pylori*. The association between blood group A and gastric cancer is stronger in males and those with diffuse-type cancer, compared to females or those with intestinal-type cancer.(Nomura, 1982; Kramer, & Johnson, 1995)

Smoking:

Carcinogen substances in tobacco can damage the lining of the stomach causing gastric cancer. The relationship between smoking and gastric cancer are dose and intensity dependent. Smoking can increase the chance of getting gastric cancer by 50 percent in men compared to the non-smoker. (Nomura, et al, 2012)

Alcohol:

Heavy alcohol consumption can increase the likelihood of getting gastric cancer especially in the non cardia region compared to moderate drinkers. This is because the ethanol from alcohol can damage the stomach mucus membrane causing the carcinogenic substances to penetrate into the mucosa and cause DNA to mutate which leads to tumour.

Anaerobic bacteria :

Dysbiosis, which is a disruption of healthy microbiota, can lead to oncogenic mucosal inflammation and metabolic dysregulation, leading to the development of cancer. Dysbiosis of the gut microbiota has been linked to gastric cancer, and although anaerobic bacteria such as Bacteroides, Bifidobacterium, Clostridium, and Peptostreptococcus mostly constitute the colonic microbiota, evidence shows that gastric carcinoma

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tissue colonisation occurs not only by intestinal flora but also by oral microbiota, including Fusobacterium, Prevotella, Porphyromonas, and Parvimonas, which mostly consist of anaerobic bacteria. Thus, anaerobic bacteria may play a potential role in the tumorigenesis of gastric carcinomas.(Thursby, & Juge, 2017)

Epstein-Barr virus infection

The Epstein-Barr virus (EBV) is a herpesvirus that contains double stranded DNA and is linked to gastric cancer. It is classified as a Group I carcinogen by the WHO and IARC and is found in all human populations. EBV is associated with Burkitt's lymphoma, Hodgkin's disease, and nasopharyngeal carcinoma, and is more prevalent in Japanese populations. The mechanism of EBV-mediated gastric carcinogenesis is unclear, but virus replication occurs in pharynx and salivary gland epithelial cells and subsequent infection of lymphoid B-cells is mediated by the interaction of viral envelope glycoproteins and CD21. Up-regulation of p53 is rarely observed in EBV-positive carcinomas, but found in over 30% of EBV-negative carcinomas, and other markers such as p27 loss, p16 loss, cyclin D1 expression and NF-κB nuclear positivity are found more frequently in EBV-positive gastric carcinomas.(Shibata, & Weiss, 1992; IARC, 1997)

Meat/ smoked food

Red meat and smoked food contain nitrates that can form into N-nitroso compounds (a type of carcinogenic substance) in the stomach. Moreover, maillard browning in red meat creates multiple carcinogenic compounds including PAHs and HCAs. These carcinogenic compounds can cause reactive oxygen species which leads to DNA damages and chronic inflammation.

***Helicobacter pylori* infection**

Pylori has been identified as one of the main causes of stomach cancer, accounting for 89% of cases of noncardia and 18% of cases of cardia. *H. pylori* was classified as a class I carcinogen by the Internal Agency for Research on Cancer (IARC,1997), an arm of the World Health Organization. A three- to six-fold increase in the risk of stomach cancer has been linked to *H. pylori* infection. The process by how *H. pylori* increases this risk is unknown, but two potential mechanisms have been considered: indirect action of *H. pylori* and direct regulation of the stomach mucosa via virulence factors including CagA and VacA. via the Correa model, which postulates that persistent stomach inflammation causes a cascade of mucosal atrophy, metaplasia, dysplasia, and ultimately cancer, chronic, active gastritis can then promote gastric carcinogenesis. (World Health Organization, 2021)

Anti-Gastric/Parietal CellAntibodies

For the Anti-Gastric, there is Antiulcer to treat and prevent duodenal and gastric ulcer illness, as well as to relieve acid reflux, esophagitis, and minor upper intestine discomforts, there is an anti-ulcer medication for the stomach.The parietal cell enzyme is the target of gastric parietal cell antibodies (GPC). A significant number of cases of autoimmune gastritis are associated with the autoantibody, and some of these patients will go on to develop pernicious anaemia.

Obesity

The effects of obesity seem relatively low compared to other obesity related cancer like colon or breast cancer. Moreover, the study in the Japanese population shows that obesity may not be the cause of gastric cancer, but it is actually the metabolic syndrome which is usually associated with obesity. (Hamaguchi, *et al*., 2020)

Clinical feature

Patients with gastric cancer often present with symptoms, but the disease is still not fully understood. Weight loss and chronic abdominal pain are the most common symptoms at the time of diagnosis, with calorie intake often being insufficient. Stomach pain is initially mild and diffuse but intensifies as the disease progresses. Other common symptoms include dyspepsia, dysphagia, vomiting, and passing dark, tarry stools. Non-specific symptoms such as anemia may also be present, indicating a late stage of the disease. In advanced cases, an epigastric mass may be felt, and additional indications of metastatic illness may include hepatomegaly, ascites, jaundice, or acanthosis nigricans. The complications of gastric cancer can include gastric outlet obstruction, iron-deficiency anemia, perforation, and malnutrition. The overall 10-year survival rate for stomach cancer is only 15%, but this is stage-dependent, with most cases

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presenting at an advanced stage with metastasis and having a survival rate of less than 5%. Additionally, it's important to note that early detection through screening and increased awareness of risk factors can greatly improve the prognosis for gastric cancer patients. (Carl-McGrath, et al, 2007)

Pathophysiology of gastric cancer

Gastric cancer usually progresses gradually and is mainly of the adenocarcinoma type, affecting 90% of patients. This cancer variant develops from the stomach's inner lining and becomes more severe as it penetrates the outer layer. Adenocarcinoma has two variants, namely, intestinal and diffuse. The intestinal type is more recognizable and treatable with drugs, while the diffuse type is linked to H. pylori infection and linitis plastica development, spreads more intensively, and is less common. Intestinal type is more prevalent in elderly men, while diffuse type is more common in women below 50 years old. (Hopkinsmedicine, 2023; Carl-McGrath et al, 2007) According to Lauren's histopathologic classification, gastric cancer has two primary histologic variants, namely, the intestinal and diffuse types. The intestinal type is the most common and is characterised by a lack of intercellular adhesions. The less frequent diffuse-type gastric cancer is associated with a germline mutation in the E-cadherin protein, leading to the absence of intercellular adhesions. CDH1 asymptomatic carriers run the chance of developing early breast cancer, and there are no obvious precancerous lesions in the diffuse variety. The intestinal type progresses from chronic gastritis to intestinal metaplasia, dysplasia, and adenocarcinoma, while the diffuse type is linked to H. pylori infection and develops into linitis plastica. Intestinal-type cancer cell lines are more sensitive to 5-fluorouracil and oxaliplatin, while diffuse-type cell lines are more resistant to cisplatin. H. pylori infection increases the risk of developing gastric cancer, especially adenocarcinoma of the distal stomach, including both intestinal and diffuse types, by about six times. H. pylori causes inflammation that leads to stomach atrophy, metaplasia, and ultimately carcinoma. However, no conclusive proof of bacterial virulence or extensive mass eradication could raise or lower the frequency of gastric cancer. Therefore, H. pylori illnesses should be screened and treated in line with current recommendations. (Lauren, et al.,1965; Tan, et al.,2011)

Epidemiology of gastric cancer in global

Gastric cancer or stomach cancer ranked 5th as the most common type of cancer and ranked 3rd in most mortality rate as of 2020. According to the Globocan report in cancer statistics around the globe there are 1,089,103 new cases and 768,793 new deaths in accord with the 2020 report. Most newer cases came from Asia with 819,944 cases, 136,038 cases coming from Europe and 97,389 cases in both North and South America; 67,617 cases came from South America and the least cases coming from Oceania with 3,330 cases. Majority of cases in Asia are from East Asia which covers 656,349 cases in accordance with the Globocan report in 2020. Most mortality cases are from Asia with 575,206 deaths, 96,997 deaths coming from Europe, 66,783 mortality in both South and North America with the majority of deaths from South America with 53,392 fatalities. And Oceania accounted for 1,862 deaths. (Sung, *et al*.,2020). Overall, it can be clearly observed that gastric cancer is the highest in Asia, especially in East Asia, and the least in Oceania.

Epidemiology of gastric cancer in Oceania

In Oceania, 3,000 cases of stomach cancer were identified amongst 250,000 cases of all cancer cases in Oceania making up 1.3% of all cancer diagnoses. 1,862 deaths from gastric cancer was reported in the 2020 Globocan reports making it the 12th deadliest cancer in the continents after Oesophageal cancer. In the 5-years prevalence of all ages, it is estimated that around 5000 people have this disease. (Sung, *et al*.,2020)

Epidemiology of gastric cancer in Asia

In Asia, there were more than 727,000 cases of gastric cancer identified in 2008, making up 11.9% of all cancer diagnoses. After lung and breast cancer, it is the third most prevalent cancer in Asia. Comparing Asia to other continents, the age-standardised rate (ASR) of incidence is greatest there (18.5%). Mortality has the second-highest ASR in Asia (13.4%), trailing only lung cancer (19.15). After breast and colorectal cancers, it is the third most common malignancy in Asia. Comparing Asia to other continents, the incidence and mortality rates of gastric cancer are also the highest in both males and females. (Matsuda, *et al*.,2013).

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Additionally, compared to other parts of Asia, Eastern Asia has greater incidence and mortality rates. The three nations with the greatest rates of gastric cancer incidence and mortality are in this region: China, Japan, and South Korea. South-Central Asia has the lowest rates. The rates are lower for females than men in each of Asia's four regions. (Yang, 2006).

Epidemiology of gastric cancer in Thailand

In 1999, gastric cancer was not among the top ten cancers in women in Thailand, but rather it was the eighth most prevalent cancer in men. For men, the expected ASR was 3.5, while for women, it was 2.8. Chiang Mai had the highest incidence rates for both men (ASR = 5) and females (ASR = 4.4) in Northern Thailand. The majority of instances of gastric cancer are adenocarcinomas. Microscopic verification from the nine cancer registries varies from 20% to 100% for women and from 32% to 95% for men. Stomach cancer is extremely uncommon before age 20; after that, it becomes more common for both sexes after age 60. (Khuhaprema, *et al*.,2013).

Gastric cancer deaths in Thailand hit 3,451 in 2020, or 0.78% of all deaths, according to the most recent WHO statistics. Thailand is ranked #141 in the globe by age-adjusted Death Rate, which is 3.41 per 100,000 of the population.

Survival

In most parts of the world over the past few decades, the mortality rate from gastric cancer has significantly dropped. (Jemel, *et al*., 2002). Nonetheless, gastric cancer continues to have a poor prognosis and a high mortality rate; it is the second-leading cause of cancer-related death globally, after lung cancer. Gastric cancer survival rates are generally greater in nations with higher incidence rates than in those with lower incidence. (Verdecchia, *et al*., 2004). This connection is mostly caused by a variation in survival rates depending on the location of the tumour within the stomach. Compared to tumours in the pyloric antrum, those in the gastric cardia had a substantially worse prognosis, with lower 5-year survival and increased operational mortality. (Fielding, *et al.*,1989).

Also, a decline in mortality has been brought on by the availability of screening for early detection in high-risk locations. Japan, a country with widespread screening initiatives, since the early 1970s, the mortality rate for men with stomach cancer has more than half. (Mondial, 2001). The 5-year survival rate is around 95% when the disease is limited to the inner lining of the stomach wall. In contrast, the US has a low 5-year relative survival rate of less than 20% with few cases being found at an early stage. (Ries, *et al*., 1997). Compared to Europe it has a range of 10% to 20% for 5-year relative survival rates for gastric cancer. (Faivre, *et al*., 1998). A US study found that people of Asian heritage had a better prognosis for gastric cancer than non-Asians, suggesting that host-related characteristics may also have an impact on prognosis. (Theuer, *et al.*,2000).

ABO blood group system

The ABO blood group system was first discovered in 1901 and consists of 4 different types of antigens, O,A,B and AB (Storry, *et al.*,2009). The production of protein consists of 3 allenes, A,B and O which are deciphered from ABO genes. The combination of these 3 alleles within red blood cells leads to 6 possible genotypes and 4 possible phenotypes. The ABO blood group system is the most widely studied system due to its phenotypes being easy to recognize. The frequency of the common ABO phenotypes varies greatly between different populations around the world. Blood group A phenotype is prevalent in Northern and Central Europe but is very rare in parts of Asia. Whereas the B phenotype is most frequent in Central Asia and almost absent in Amerindians. The O blood group is the most common blood group found globally, with Native American Indians being almost exclusively O blood group. Furthermore, parts of Africa and Australia also show high amounts of O blood group. Synthesis of blood group antigens needs at least 2 steps. The first is the synthesis of H antigen, the antigen responsible for the O blood type. The second step is the synthesis of either A or B antigen. The H antigen is formed by the addition of fucose in a 1,2 linkage to a terminal galactose on a type 1-4 chain. After the H antigen has been formed, the A and B transferase and use the H structure to synthesise A and B antigens type 1-4 chains (Yamamoto, 2004) (Table 1). Ever since this blood group was discovered, there have been many efforts to find a link between ABO blood groups and abnormalities or different infectious diseases including tumours and cancers. This is due to the possible connection between the different antigens

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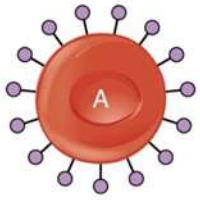
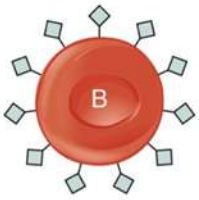
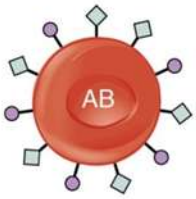
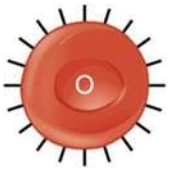
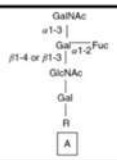
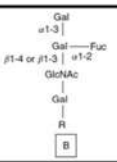
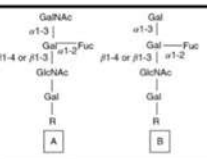
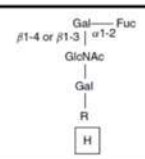
and the severity and growth of certain diseases. Through research, it has shown that there is a relationship between certain diseases and the ABO blood group. This may be because of the role that these antigens play in many of the body's processes including the movement of cells, cell division, inflammation etc. These results may indicate the possible connection between ABO blood groups and the severity of many diseases and infections.

Table 1. ABO blood group and its characteristics

	Blood Type			
	A	B	AB	O
Red Blood Cell Type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red blood Cell				
Blood Types Compatible in an Emergency	A, O	B, O	A, B, AB, O (AB^+ is the universal recipient)	O (O is the universal donor)

Association of ABO blood group system and gastric cancer

Patients with type A blood had a much-increased risk of developing gastric cancer than patients with other blood types, suggesting that type A blood is likely to have an effect on the pathogenesis of gastric cancer. The data do support the theory, which states that those with blood types A have higher probability of developing gastric cancer (Table 2). In conclusion, the current research verified that people with blood group A have a higher risk of developing gastric cancer than people with other blood types. An increased chance of H. pylori infection may contribute to blood group A. According to this research, the host must have a genetic susceptibility to gastric cancer. However, more research is required to determine the precise molecular process underlying the association between ABO blood groups, H. pylori infection, and gastric cancer.

Table 2 Association of ABO Blood Group with Gastric Cancer

S.N	Cancer	Sample size	Blood group association	Country and state	References/ study

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1	Gastric cancer	1045	A	Ruijin hospital, Shanghai	Zhiwei Wang *et. al.*, 2012.
2	Prognosis analysis of gastric cancer	488	A	Xinjing	Xiao-jie Sun et. al., 2011.
3	Chronic atrophic gastritis	241	A	Japan	Atsuko shibata et. al., 2002
4	Premalignant gastric lesions	160	A	turkey	Kadir, Murat.,2020
5	Risk of cancer among middle-aged people	3124	A	Taiwan	Ling-Tzu HSIAO et. al., 2015
6	Risk of gastric cancer	4617	A	Korean	Nasser, Bander., 2020
7	Risk of gastric cancer	897	A	China	Yu et. al.,2012
8	ABO blood group with gastric cancer	1412	A	China	Ye-QIONG xu et.al., 2016
9	ABO blood group types with cancer risk	243	A	Sir Sunderlal hospital, India	Singh, et.al., 2019
10	Rick of esophageal and Gastric cancer	1189	A	China	Chen, et.al., 2021

The role of pathogenic mechanism of ABO blood group in gastric cancer

The underlying mechanisms by which the ABO blood group or the closely linked genetic variants of the ABO locus may interplay with cancer development and progression are still poorly understood and remain the topic of research. One possible hypothesis encompasses a dysregulation of the enzymatic activity of the ABO glycosyltransferases, which are specifically involved in the processes of intercellular adhesion and cellular membrane signalling as well as in the immune response to the host. The alteration of these surface molecules may promote the process of malignancy, through a mechanism similar to the well-known role played by the ABO glycosyltransferases in modulating the circulating plasma levels of von Willebrand factor and the consequent increased risk of venous thromboembolism. This association is particularly interesting, also considering that von Willebrand factor was recently found to be an important modulator of angiogenesis and apoptosis, which, in turn, are processes involved in tumorigenesis. Alterations in the host inflammatory state due to ABO blood group antigens provide a further potential mechanism by which blood type may influence the progression and spread of malignancy. Recent studies reported an association between polymorphisms at the ABO gene locus and circulating levels of tumour necrosis factor-alpha, soluble intercellular adhesion molecule (ICAM)-1, E-selectin and P-selectin. All these adhesion molecules are important mediators of chronic inflammation and immune cell recruitment. They may, therefore, provide a biological basis for the postulated influence of ABO on cancer survival, by directly linking ABO blood group and tumour initiation and spread. The expression of soluble ICAM-1, which inhibits lymphocyte attachment to endothelial cells by binding to the ICAM ligands on circulating cells, is significantly reduced in patients with non-O blood group (particularly blood group A) compared to the expression in those with blood group O. Since some

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cancer cells use similar mechanisms for adhesion to endothelial cells and subsequent metastatisation, the decreased soluble ICAM levels in patients with non-O blood groups may promote metastatic spread of tumours. Another hypothesis to explain the relationship between ABO blood group and gastric cancer development involves type A blood patients having larger salivary levels of substance A. The presence of substance A in saliva and gastric secretions might affect the gastric mucosa and raise the risk of a malignant transformation. In support of this hypothesis, a number of studies showed decreased survival in non-O blood type cancer patients and a favourable prognosis in those carrying O blood type.(Wang, et al. 2012) H. pylori infection is suggested to be a factor in the association between ABO blood antigens and the emergence of gastric cancer. H. pylori plays an important role in the development of gastric cancer. The International Agency for Research on Cancer has designated Helicobacter pylori as a class 1 carcinogen. According to experimental research, the particular blood type antigen, which is produced by blood type genes at 19q13, facilitates H. pylori's adhesion to human gastric mucosa. (Huang, et al., 2017) These antigens are present on a variety of cells, including those in the stomach lining. By interacting with a particular protein on the bacterium's membrane, the Lewis b antigen (Leb) and associated fucose residues on ABO antigens give a site for H. pylori to bind to and produce chronic inflammation. Furthermore, the association of H. pylori as a risk factor for the development of gastric cancer is mediated by virulence factors mostly produced by cagA strains. H. pylori is a gram-negative bacteria that can be classified into strains that are positive for either the vacuolating cytotoxin (VacA) or the cytotoxin-associated antigen (CagA). A significantly elevated risk of gastric cancer is suggested by H. pylori that is CagA-positive. The H. pylori adhesion molecule system aids in the colonization of the bacteria in the stomach mucosa. Blood group antigen binding adhesion A is the most significant adhesion molecule (BabA). Gastric disease risk is increased by H. pylori adhesion. Animal studies demonstrated that BabA might induce the production of additional interleukin-8, pro-inflammatory cytokines, and pre-cancer-related substances from the inflammatory cells. The increase of pro-inflammatory cytokines in individuals with chronic gastritis may have a significant clinical impact on gastric carcinogenesis since the inflammatory response to H. pylori infection plays a significant role in cellular proliferation and gastric mucosal degradation. (Wang, et al., 2012) The ABO genotype and H. pylori infection status, however, were found to be independent risk variables in the study's analysis and did not appear to interact. In separate analyses with the control group, the relationships between the ABO genotype and H. pylori infection as well as the prevalence of certain stomach diseases were not adequately evident. More study is necessary to determine whether interactions between ABO blood antigens and H. pylori or some other independent mechanism affect the development of gastric cancer.

Survival rate of gastric cancer and ABO blood group

Based on the study from 2020, people with a type O blood group have an overall higher survival rate than non-type O blood group. (Yu, et al.,2020). But, according to a 2023 study on prognostic relationships between the ABO blood groups shows that AB blood groups have the highest overall survival rates than any other types that is followed by blood group B and O which are close in terms of overall survival rate. (Tuncel, et al.,2023). According to Qiu and co worker., there is insufficient evidence to suggest that blood type is a reliable prognostic indicator for patients with gastric cancer. While previous studies with large sample sizes have produced inconsistent conclusions, most have suggested that ABO blood group may affect cancer prognosis. Therefore, further investigation is necessary to determine the relationship between ABO blood group and cancer prognosis (Qiu, et al., 2011. However, early detection of gastric cancer is low, resulting in many patients presenting in advanced stages of the disease, reducing the effectiveness of treatment options. Consequently, the overall prognosis for gastric cancer patients is unfavourable. Identification of risk factors is a must to link with the development and progression of gastric cancer. Eventually this may lead to improved preventive measures and treatment options. The onset and progression of gastric cancer result from a combination of genetic and environmental factors.

Conclusion

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Gastric cancer is still a leading cause of cancer-related deaths globally. Unique epidemiologic characteristics of gastric cancer include significant geographic variation, divergent time trends, and variations according to ethnicity, sex, and socioeconomic position. Dietary factors and the *H. pylori* infection seem to be the primary contributors to gastric cancer. Including blood types can be used to forecast and assess prognosis in patients with metastatic gastric cancer. We found that patients with blood group A had a higher likelihood of developing gastric cancer and a worse prognosis, while patients with blood group AB had a better prognosis and a higher chance of surviving the disease. The ABO blood groups should be taken into account when determining a patient's danger, along with other risk factors. The blood group of a patient with gastric cancer can be used as a prognostic factor in regular clinical practice because it is an easy, accessible, affordable, and useful technique. Therefore, main prevention strategies going forward should concentrate on high-risk populations' modifiable risk factors. Furthermore, research is necessary to investigate the potential use of ABO blood group as a prognostic indicator for patients with gastric cancer.

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