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A Clinico-pathological Correlation of Carcinoma Stomach and ABO Blood Group

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Abstract

Introduction: *Stomach cancer related to higher rate for blood group A over other ABO types, a prospective assessment of relation between blood group and carcinoma stomach was performed with a view to state the role of ABO blood group in the development of gastric cancer with relationship of clinico-pathological variation. This study sought to investigate the relationship between ABO blood groups and the risk of gastric cancer as well as clinical pathological parameters.* **Materials and Methods:** *A Prospective random observational study carried between October 2005 to September 2006 in Dhaka Medical College Hospital, Department of Surgery & Radiotherapy. Maximum patients admitted in the surgery units with diagnosed case of carcinoma stomach were taken as sample or study population & rest attended in radiotherapy department in DMCH.* **Results:** *Among the 70 cases the mean age is 44.3(18-65) (M/F=4:1) years. All the information and data taken from Hospital records and patients themselves or first degree relatives. Results Blood group B-42.85%, A-34.28%, O- 15.71% only 11.42% gave positive family history. Histopathological report show's Adenocarcinoma 95% and among them blood group B 40% and A 31.42%. The differentiation of carcinoma stomach are categorized as Grade-I well differentiated, 37.14% cases moderately differentiated 15.71% and poorly differentiated 45.71%. Among them blood group B is more in case of poorly differentiated carcinoma 25.71%, blood group A is more in well differentiated carcinoma 17.14%.* **Conclusion:** *Blood group 'A' has an established relationship with carcinoma stomach. In this study it is found that blood group 'B' is more associated with carcinoma stomach and with poorly differentiated adenocarcinoma.*

Keywords: Carcinoma Stomach, ABO Blood Group.

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Introduction:

Among the malignant tumours' that occur in stomach, carcinoma is overwhelmingly the most important. Its incidence varies widely. In order of frequency the incidence of malignant tumours of stomach approximately are as follows:carcinoma-90-95%,lymphoma 4%,Spindle cell Tumours 2%, Carcinoid 3%. Gastric carcinoma is a wide spread disease. It is particularly high in Japan, Chile, Costa Rica, Colombia and considerably lower in USA, UK, Canada, Australia, Greece, New Zealand, Sweden and Holland. Gastric cancer is the second most common cause of cancer death worldwide about one million patients are newly diagnosed with gastric cancer each year, with 700,000 deaths each year[1].

During the past 5 decades, incidence and mortality of gastric carcinoma has been declined. Nevertheless gastric carcinoma remains a formidable challenge since its over all five year survival rate still continued to be dismally poor. It is a leading cause of all cancer related deaths. It is one of the "captains of men of death[2]. In USA the mortality rate from gastric cancer has dropped from about 30 to 6 per 100000 for men and from 21 to 4 per 100000 for women during last 50 years. In Japan the percentage in mortality surpassed that in incidence. It is postulated that the mass-screening program has had some impact. It is known that gastric cancer can be caused by the interaction between environmental factors and genetic variations[3-5].

Although improvements in nutrition, occupations and socio-economic class have been frequently suggested, the reasons for the dramatic decline in the incidence of stomach cancer remain unclear[6].

There are some preexisting conditions that culminate to gastric carcinoma. Statistical evidence suggests that chronic atropic gastritis, pernicious anaemia, adenomatous polyp, hypertrophic gastropathy, achlorhydria and hypochlor hydria as well as preexisting gastric ulcer are the precancerous lesions[1]. Pernicious anaemia: Fisk of gastric carcinoma was first suggested by Zamcheek et al. in 1955. They concluded that approximately 10% of patient develop gastric carcinoma. Presumable the achlorhydria/ hypochlorhydria associated with pernicious anaemia leads to malignant change[7]. Gastric

neoplastic polyp: Neoplastic polyp have (40-66%) of undergoing malignant change. Incidence of cancer is increased in polyps larger than 2 cm in diameter. Huppler and associates reviewed the records of 465 patients with gastric polyps seen at Mayo Clinic 300 patients were operated and 20% of polyp of these patients was malignant, 80% of the patients were achiordydric. Age incidence of neoplastic polyp was between fifty and seventy years[8]. Previous gastric operation: Gastric surgery for benign condition increases the risk of gastric cancer by two- to six-folds. Most cases have occurred after Billroth-II anastomosis, 20 years after the original surgical procedure[9].

The discovery of blood groups in human beings by the Austrian scientist Carl Landsteiner in 1900 was a land mark in the history of medicine for which he was given the 1930 Nobel Prize in Medicine/Physiology. In his study involving[10]. individuals of his laboratory, he indicated three blood groups based on the reactions of different combinations of cells and sera. He named these blood groups as A, B, and C (which later became group O). Apparently, none of the staff of Landsteiner's laboratory had the less common blood group AB which was later reported by other Austrian investigators[11].

The first attempt to correlate a polymorphic system with disease susceptibility was made following the discovery of red blood cell groups. On the assumption that such polymorphisms must be maintained by selection, a search for associations between blood groups and specific diseases was initiated. The first such association was found between blood group A and stomach cancer in 1953[12]. There have been many other studies since that time, showing varying levels of risk of stomach cancer for type A. The role of blood groups in predisposition to various diseases has been studied and reported[13]. One study done in China in 1994 on a population group that has very high stomach cancer rates overall, does show a higher rate for blood group A over other ABO types, but also shows an elevated rate for any ABO type if a family member had stomach cancer, in fact, the odds ratio was much higher for having a parent who had stomach cancer than for being the A blood type[14,12] were the first to notice the correlation between gastric cancer and blood group A[15]. Since then, the relationship between ABO blood groups and carcinogenesis or progression of human tumors has been reported by many investigations, including increased breast cancer risk in blood group A[16]. However, the results regarding the relationship between blood group A and gastric cancer were inconsistent[17–19].

Many studies have addressed the correlation between ABO antigen a development of gastric cancer but most of these have indicated correlation between sporadic cases of gastric cancer and blood group A. This association further supports the role of genetic factors in the development of gastric cancer.Gastric carcinoma develop in patients with blood group-A (Japanese however claim blood group-B).

Blood type A is more strongly associated with diffuse gastric histopathological type of cancer than intestinal type[20].

Since the association between blood group A and gastric cancer was reported in 1953 and the relationship with blood groups and incidence clinicopathological parameter and prognosis had been studied in many cancer and other disease. However there is no consistent result. Additionally ABO gene are distributed differently among socioeconomic group. We know that socioeconomic status is one of the risk factors for disease. Blood group related antigens A and B in gastric cancer expressed in intestinal and diffuse type of carcinoma differ significantly in patient of blood group A and blood group B.Thus another observation gave only partial support for the hypothesis that the association between ABO blood groups and gastric carcinoma is dependent on the antigenicity of the neoplasm.Thus a perspective assessment of relation between blood group and ° carcinoma stomach was performed with a view to state the role of ABO blood group in the development of gastric cancer with relationship of clinicopathological variation.

Aims And Objectives 1-To study the relationship between ABO Blood Group with Clinico-pathological types of carcinoma stomach. 2-To see the incidence and relation of Blood Group-A or Blood Group B and histopathological types of gastric cancer.

Materials and Methods:

This is a prospective random observational study carried between October 2005 to September 2006 in Dhaka Medical College Hospital, Department of Surgery & Radiotherapy. Maximum patients admitted in the surgery units with diagnosed case of carcinoma stomach were taken as sample or study population & rest attended in radiotherapy department in DMCH.

All patients with gastric carcinoma irrespective of the site and histological variation, in Dhaka Medical College Hospital in Surgery department and radiotherapy department were prospectively assessed for the association with ABO blood group. Data about age sex, ABO blood type, Endoscopic diagnosis, histopathological variation, operability and inoperabiity included. Clinical and histopathological diagnosis are available, differentiation of carcinoma are categorized grade-I (well differentiated) to grade III (Poorly differentiated). All patient's medical record including operation note, histopathological reports were reviewed.

For all 70 cases a standard protocol according to the data sheet were maintained. The collected data were analyzed.

Criteria for selection: 1. All histopathologically diagnosed cases of carcinoma stomach were included in study period. 2. Only the ABO blood group was considered in the study. 3. All operable and inoperable cases were included. Criteria for exclusion: Other malignant tumors of the stomach histopathologically proved.

Results:

Out of 70 cases, 8(11.42%) cases were found in the age group below 40 years, 36(51.42%) cases in the age group of 41-50 years, 23(32.85%) cases in the age group of 51-60 years and only 3(4.28%) cases beyond the age of 60 years. Incidence of gastric carcinoma predominate in male. In this series of 72 cases the male to female ratio 4:1. Out of 70 patients, only 8 (11.42%) patients had positive family history of carcinoma stomach. Here ABO blood distribution. Out of 8 cases, 6 cases had same blood group, group-A and others blood group-O. Six male and two female patients of the present series gave history of peptic ulcer. None could show any evidence of pernicious anemia, atrophic or benign stomach tumour. Two patients gave positive history of gastric surgery.

Table-I: Blood group of patient (n=70)

Blood group	No. of patients	Percentage (%)
B	30	42.85
A	24	34.28
O	11	15.71
AB	5	7.14

Symptom

It is to be mentioned that most of the patients in this series attended in DMCH for surgical treatment in Department of Surgery and for Chemo Radiotherapy treatment in Department of Radiotherapy and all the cases were established cases of carcinoma. The mode of presentation in different patients is shown in Table-II.

Table-II: Leading symptoms observed in patients (n=70).

Symptoms	No. of patients	Percentage (%)
Epigastric discomfort	68	97.14
Epigastric pain not responding to treatment	42	60
Anorexia	65	92.85
Loss of weight	70	100
Loss of appetite	65	92.85
Vomiting	69	98.57
Dysphagia	5	7.14
Lump in epigastric	31	44.28
Haematemesis and meleana	7	10
Fatigue and tiredness	49	70
Acute abdomen with all the features of perforation of hollow viscus	2	2.85
Anaemia	68	97.14
Weight loss	68	97.14
Dehydration	54	77.14
Ascites	6	8.57
Oedema	3	4.15
Jaundice	6	8.57
Virchow's gland	5	7.14
Umbilical nodule	2	2.85
Subcutaneous nodule	1	1.42
Trousseau's sign	1	1.42
Visible peristalsis	21	30.0
Palpable mass	27	38.57
Succussion splash	42	60.0

Table-II shows that anaemia and weight loss were present in all cases (97.14%), Dehydration of some degree was present in 77.14% patients, palpable mass in 58.69%, ascities 8.57% and oedema in 8.57%, jaundice in 4.16%, tenderness in epigastrium in 5%, visible peristalsis in 30%, positive succussion splash in 60%. Trousseau's sign in 1.13%.

All routine investigations were done with special attention to haematological percent, ESR and x-ray chest, urine R/M/E shows Hb%- within 41-50% were 69.44% cases. Below 40% Hb were 13.8%, ESR above 33 (95.55%) cases, no chest involvement urine abnormality.

Endoscopic examination of stomach and duodenum-

Out of 70 cases in the present study, endoscopic examination was done in all cases. 34 cases showed presence of growth at the antrum, 15 cases at the body, 8 cases at the fundus and 6 case at the cardiac end of stomach and 7 cases ulcerative lesion at the antrum and body. Biopsy taken during endoscopic examination was sent for histopathological examination. USG was done to detect intra-abdominal metastasis, hepatic lesion in 08 cases (11.42%). Ascites 6(8.57%) and enlarged regional lymph node 32(45.71%) were found, 21(30%) patients had normal findings on USG. 3 patients had misssed there USG report.
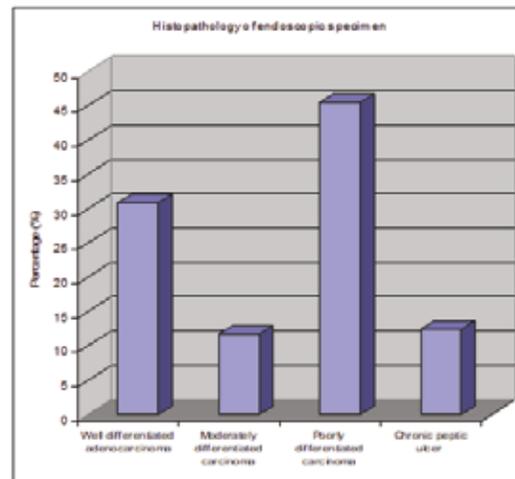

Figure-1: Histopathology report of endoscopic biopsy specimen (n=70).

Here the peroperative findings were shown 60 cases out of 70 cases. 45 cases out of 60 were taken from department of surgery, 15 cases were taken from radiotherapy department. Operative findings of this 15 cases operated outside DMCH were collected from discharge paper.

Table-III: Peroperative findings (n=60)

Laparotomy findings	No. of patients	Percentage (%)
Mobile growth involving the serosa	31	51.66
Fixed growth to the posterior abdominal wall	21	35.00
Ascites	6	10.0
Involvement of regional lymph nodes	57	95.00

Laparotomy findings	No. of patients	Percentage (%)
Involvement of liver	8	13.33
Discrete peritoneal seeding	3	5.0
Involvement of pelvic peritoneum	3	5.0
Location of primary tumour		
Antrum	33	55.0
Body fundus	21	35.0
Cardiac	6	10.0

Table-IV: Histopathology of resected specimen/biopsy (n=60).

Histopathological report	Number of patients	Blood group				Percentage (%)
		A	B	O	AB	
Adenocarcinoma	57	22	28	5	2	95
Squamous cell carcinoma	3	2	1	0	0	5

In this series, out of 70 patients 60 were operated and sent for biopsy, 57 (95%) were adenocarcinoma, 3(5%) squamous cell carcinoma.Out of total number of 70 patients 60 patients were operated, So, in 60(95%) patients histopathologically were found as adenocarcinoma and 5% squamous cell carcinoma. This 5% cases involved cardiac end of the stomach. Possibly this 5% growth develop from lower end of the esophagus-extending and involving the cardiac end of the stomach.

Table-V: Relation of ABO blood group degree of differentiation of adenocarcinoma (n=67).

Blood group	Well differentiated	Moderately differentiated	Poorly differentiated
A	11 (16.41%)	2 (2.98%)	9 (13.43%)
B	9 (13.43%)	2 (2.98%)	18 (26.86%)
O	4 (5.97%)	3 (4.27%)	4 (5.97%)
AB	1 (1.49%)	3 (4.47%)	1 (1.49%)

B group is worse and more in poorly differentiated about 26.86% and A group is more well differentiated 16.41% rest.

This series, surgery was done in 60 out of 70 patients (including laparotomy and biopsy, palliative surgery and curative resection). Among these patients growth was resectable in 43.33% cases and remaining 50% cases growth was unresectable. Among the non-resectable group some form of palliative surgery (by pass) was done in 49% cases, and remaining 6.67% cases no surgical treatment was done. Conservative treatment chemotherapy and radiotherapy were given 14.28%.

Discussion:

From clinical practice it is quite evident that the incidence of this diseases is also significantly high in Bangladesh but no data about the incidence is available. In a country like us, it is very difficult to diagnose gastric cancer at an early stage by implementing mass screening program (Moreover it will not be cost effective in countries where gastric cancer incidence not so high as in Japan). In this study, it was evident that, (In our country) most of the patient coming to the hospital in a very advanced stage, when there is very little to be done for them.

In the present study, 70 cases were studied which were diagnosed as carcinoma of stomach and 45 cases had been admitted into surgical units of Dhaka Medical College Hospital and rest 25 patients from radiotherapy in Dhaka Medical College Hospital. We have tried to detect mode of clinical presentation and preoperative staging by some imaging studies within our limited resources and correlated this with the operative findings and degree of differentiation of the carcinoma stomach and ABO blood group.

Age and sex factors

Age and sex were important factors for incidence and the time of presentation of the disease. It may occur at any age but rare before the age of 30 years. In this study 61 cases (84.72%) were found in between 40 to 60 years of age, 8 cases (11.11%) below 40 years and 3 cases (4.16%) beyond 60 years of age. Only one case was found at the age of 27 years. Most of the cases were between 41-60 years age group[21]. So age is one of the determining factor of presentation as well as planning of treatment. Here this study also correlates with these findings. Overall males are three times more commonly affected than female. In this study it is found. Male: Female: 4:1.

Family history

Genetic make-up passively have some relation with gastric cancer, but it is not well established. In the present series, out of 70 cases only 8(11.42%) had positive family history of gastric carcinoma. Among the 8 cases 6 cases had same blood group 'A' and 2 cases had blood group 'O'.

Blood group

Aird[12] found a higher incidence of gastric carcinoma in people with blood group 'A'. In this series highest incidence of gastric carcinoma was found in blood group 'B' i.e. 30 cases (42.85%) and the next blood group was 'A', 24 cases (34.28%), O 11(15.71%), AB 5(7.14%). Yet not established the ABO blood group A, B is the risk factor for ca-stomach.

Presentation

Carcinoma stomach is a very difficult disease to diagnose early, not only because of the diversity of its presentation, but also because of the time lag between the commencement of the growth and the appearance of symptoms. All patients in this series came with symptoms and were admitted in hospital as suspected case of carcinoma except two patients who were admitted from emergency as acute abdomen due to perforation of hollow viscus.

In the present series, 70 cases were studied. Out of 70 cases, 68 (97.14%) cases complained of epigastric discomfort, 42 (60%) cases noticed epigastric pain, 65 (92.85%) cases anorexia, 65 (92.85%) cases developed loss of appetite, 70 (100%) cases lost their weight,

68 (98.57%) cases developed vomiting, 5 (7.14%) cases complained of dysphagia, 31 (44.28%) cases noticed lump, haematemesis and melaena developed in 7 (10%) cases. Fatigue and tiredness was present in 49 (70%) cases.

Physical findings- Mount ford[22] found approximately 60% of the patients have palpable mass in the upper abdomen indicating advanced growth and 41% patients present with anaemia. In the present series 66% patients showed epigastric tenderness, 58.69% palpable mass, 97.14% patients with anaemia, 8.57% patients with ascites, 8.57% patients with jaundice, 7.54% patients with Virchow's gland, 11.11% with enlarged hard liver. Generally patients of gastric carcinoma presents with anaemia in 97.22% cases, raised ESR in 80% of cases.

Gastroscopic findings

Gastroduodenoscopy is a valuable aid in the diagnosis of early cases of gastric cancer. It is evident that endoscopy with biopsy is much more efficient than roentgenography in detecting minute gastric cancers and is currently to be over 90 percent accurate in diagnosing advanced gastric cancer. Grossen ManMB[23] showed, distribution of the primary site of malignant gastric tumours in 200 surgical specimen about 48.5% in antrum, 18% in body, 12% in fundus, 4.5% in cardia, 8.6% diffuse and 3.5% in multile site. Almost half occur in the distal antral region of the stomach. Now the proximal stomach is the most common site of gastric cancer in the UK, but carcinoma of the distal and body of the stomach is most common in low socioeconomic group.Of the 70 patient in this series, 34 patients showed presence of growth in antrum, 23 body and fundus, 6 cardiac.

Histopathologic result of endoscopic biopsy reveals adenocarcinoma in 63(90%). Among this 31(44.28%) poorly differentiated, 11.42% moderately differentiated and 30% well-differentiated adenocarcinoma were found. 7(10%) cases shows chronic peptic ulcer, this 10% after laparotomy and specimen/biopsy histopathology proved to be adenocarcinoma.So in a significant number of patients endoscopic biopsy and histopathology may not reflect the true disease. Status resulting high percentage of false negative results. So in clinically and endoscopically suspected cases if endoscopic biopsy histopathology report are found in consistent, then re-endoscopy and biopsy should be considered to achieve the correct diagnosis.

Operative staging and surgical treatment

Nodal status in gastric carcinoma is not only related to prognosis but also to the extent of nodal dissection. Nodal status can be diagnosed early by Frozen section, involved lymph nodes often over looked Sentinel lymph node mapping was accurate in predicting nodal status in patients with early stage gastric cancer.Total gastrectomy with D_2 dissection is the standard treatment in Japan for early upper third gastric cancer. But it is shown that proximal gastrectomy for early upper third gastric cancer can be performed safely with an excellent cure rate.In this series, out of 70 patients, 60(85.71%) were underwent surgery. Rest 10(14.27%) were treated conservatively. Among these none in stage I and II, 28 cases (39.31%) in stage III, 14 cases (30%) in stage IV were found peroperatively. Unfortunately, the vast majority of patients seen outside Japan with advanced gastric cancer. In over 50 percent of patients, the tumour is no longer localized when first identified and gastric resection is only moderately beneficial in most of their cases. However, as was true in Billroth's time, surgical resection of the growth with healthy margin is still the method of choice to give benefit to resectable cases. Though majority of our patients of carcinoma stomach present to us at advanced stage exploration was done in all the cases for possible palliation and to do preoperative staging as well.

328 patients were reviewed retrospectively with Histologically confirmed gastric adenocarcinoma diagnosed by Cunningham D, Hde D,[24] between 1974 and 1984. Of these patients, 128 (39%) had a curative resection, 32 (9.8%) had palliative resection, 33 (10%) had a gastrojejunostomy, 26 (79%) had a elestin tube inserted, 38(17.7%) had lapartomy alone, 51 had no surgical proceures. In this series 60 patients out 70 patients underwent operative treatment finding shows- involvement of regional lymph node were in 95% cases, ascites in 10% cases, liver involvement in 13.33% cases, discrete peritoneal seedling in 5% of case and involvement of pelvic peritoneum were in 5% of cases. Location of the primary tumour antrum 55% boody fundus 235% cardiac 10%.

Histopathology

Microscopically, nearly all gastric cancers were of the adenocarcinoma type varying only in the degree of differentation. Pathological staging of carcinoma stomach depends on essential part of the operative strategy and histopathological reports from resected specimen[25] showed 3 cases (3.4%) in stage-I, 23 cases (26.4%) in stage-III, 25 cases (28.7%) in stage-III, 36 cases (41.3%) in stage IV among 87 cases.In this series 95% patients had adenocarcinoma. 5% squamous cell carcinoma, among the adenocarcinoma 57(95%) cases, Poorly differentiated were found in 53.33%, moderately differentiated in 14.92%, and well differentiated 37.31%. It is generally agreed that, the prognosis is worse in the poorly differentiated adenocarcianoma and the relationship of AB0 blood group that well differentiated adenocarcinoma, A (16.42%), B-13.43%, O- 5.97%, poorly differentiated adenocarcinoma, B– 26.86%, A – 13.43%, O- 5.97%, AB-1.49%. Among the squamous cell carcinoma 5% cases shows 2(66.66%) cases were A group and 1(33.33%) were B group. Extent of association & risk factor was not established that AB0 blood group and carcinoma stomach. This series blood group B predominant risk factor of

development of poorly differentiated adenocarcinoma A was the well differentiated carcinoma. May this relationship defends on race and geographic variations and not to correlate with the establish risk factor of A blood group.

Conclusion:

Carcinoma stomach is one of the commonest malignant disease with high mortality. The only treatment modality to cure the disease is a radical resection followed by chemotherapy. So, if the disease can be detected at an early stage, a better result can be obtained. But most of the cases in our country are diagnosed at an advanced stage. So the identification of risk factors is very important. This study was targeted to identify the relationship of ABO blood group with carcinoma stomach and also its relationship with clinical staging. In western countries blood group 'A' has an established relationship with carcinoma stomach. In this study it is found that blood group 'B' is more associated with carcinoma stomach and with poorly differentiated adenocarcinoma. But the relationship is not yet established in our country. So, we suggest a larger study to be performed including all possible cases of carcinoma stomach in all the Medical College Hospitals and Medical Institutes.

Conflict of Interest: None.

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