

CLINICO PATHOLOGICAL ASSESSMENT OF GASTRIC CANCER IN BIHAR REGION

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Abstract

Gastric cancer has been one of the leading causes of cancer-related mortality over the past century. Today it is the 4th most common cancer in the world. Surgery remains the only major curative option. Majority of these cancers are found to be unresectable on laparotomy. Most gastric cancer patients are diagnosed with advanced disease with the development of distant metastases hence assessment of prognostic markers in these patients should be done. Hence based on above condition the present study was planned for Clinico Pathological Assessment of Gastric Cancer in Bihar Region.

The present study was planned in Department of Pathology, Indira Gandhi Institute of Medical Science, Patna, Bihar, India. The present study was planned from duration of June 2018 to December 2018. In the present study 50 cases of adenocarcinoma of stomach were enrolled and evaluated. The patients were diagnosed on clinical, radiological, endoscopic examination with confirmation by histopathological examination of either endoscopic biopsy or the resected specimen. The resected gastrectomy specimens were examined grossly and tumour location, tumour dimensions, extent of tumour invasion, metastasis to lymph nodes, number of lymph nodes involved, abnormality in surrounding mucosa were recorded. Gastric cancer is second most common cancer in male and fifth most common amongst females in East and Central Asia. The incidence of gastric cancer is twice as much in men as in women. Majority of cases had history of tobacco consumption, which clearly indicates the role of tobacco in causation of stomach cancer. Weak relation was seen in alcohol consumption. Screening of asymptomatic people in a high risk area may be useful in early detection of disease. Efforts to detect cancer early in developing countries would go a long way in reducing the disease burden and improving the outcome.

Keywords: Gastric cancer, Mucinous adenocarcinoma, Tobacco, Metastasis, etc.

Introduction

Gastric cancer is the sixth most common cancer and the third most common cause of cancer-related death in the world. [1] Although rates are low in North America and Northern Europe—in the United States, stomach malignancy is currently the 15th most common cancer [2]—the disease remains difficult to cure in Western countries, primarily because most patients present with advanced disease.

Gastric cancer was once the second most common cancer in the world. In most developed countries, however, rates of stomach cancer have declined dramatically over the past half century. In the United States, stomach malignancy is currently the 15th most common cancer. [2]

Decreases in gastric cancer have been attributed in part to widespread use of refrigeration, which has had several beneficial effects: increased consumption of fresh fruits and vegetables; decreased intake of salt, which had been used as a food preservative; and decreased contamination of food by carcinogenic compounds arising from the decay of unrefrigerated meat products. Salt and salted foods may damage the gastric mucosa, leading to inflammation and an associated increase in DNA synthesis and cell

proliferation. Other factors likely contributing to the decline in stomach cancer rates include lower rates of chronic *Helicobacter pylori* infection, thanks to improved sanitation and use of antibiotics, and increased screening in some countries. [5]

Nevertheless, gastric cancer remains difficult to cure in Western countries, primarily because most patients present with advanced disease. Even patients who present in the most favorable condition and who undergo curative surgical resection often die of recurrent disease. However, two studies have demonstrated improved survival with adjuvant therapy: a US study using postoperative chemoradiation [6] and a European study using preoperative and postoperative chemotherapy. [7]

The stomach begins at the gastroesophageal junction and ends at the duodenum. The stomach has three parts: the uppermost part is the cardia; the middle and largest part is the body, or fundus; and the distal portion, the pylorus, connects to the duodenum. These anatomic zones have distinct histologic features. The cardia contains predominantly mucin-secreting cells. The fundus contains mucoïd cells, chief cells, and parietal cells. The pylorus is composed of mucus-producing cells and endocrine cells.

Externally, the peritoneum of the greater sac covers the anterior surface of the stomach. A portion of the lesser sac drapes posteriorly over the stomach. The gastroesophageal junction has limited or no serosal covering.

The right portion of the anterior gastric surface is adjacent to the left lobe of the liver and the anterior abdominal wall. The left portion of the stomach is adjacent to the spleen, the left adrenal gland, the superior portion of the left kidney, the ventral portion of the pancreas, and the transverse colon.

The site of stomach cancer is classified on the basis of its relationship to the long axis of the stomach. Approximately 40% of cancers develop in the lower part, 40% in the middle part, and 15% in the upper part; 10% involve more than one part of the organ. Most of the decrease in gastric cancer incidence and mortality in the United States has involved cancer in the lower part of the stomach; the incidence of adenocarcinoma in the cardia has actually shown a gradual increase.

Ooi et al identified three oncogenic pathways that are deregulated in the majority (>70%) of gastric cancers: the proliferation/stem cell, NF-kappa β , and Wnt/beta-catenin pathways. Their study suggests that interactions between these pathways may play an important role in influencing disease behavior and patient survival. [8]

The intestinal type of non-cardia gastric cancer is generally thought to arise from *Helicobacter pylori* infection, which initiates a sequence that progresses from chronic non-atrophic gastritis to atrophic gastritis, then intestinal metaplasia, and finally dysplasia. This progression is known as Correa's cascade. In a population-based cohort study, Swedish researchers found that after a 2-year latency, patients with precancerous gastric lesions were at higher risk for gastric cancer than the general Swedish population, and that risk increased steadily with progression through Correa's cascade. The researchers estimated that the 20-year gastric cancer risk in patients with particular gastroscopy findings was as follows [9] : Normal mucosa – One in 256; Gastritis – One in 85; Atrophic gastritis – One in 50; Intestinal metaplasia – One in 39; Dysplasia – One in 19.

Understanding the vascular supply of the stomach allows understanding of the routes of hematogenous spread. The vascular supply of the stomach is derived from the celiac artery. The left gastric artery, a branch of the celiac artery, supplies the upper right portion of the stomach. The common hepatic artery branches into the right gastric artery, which supplies the lower portion of the stomach, and the right gastroepiploic branch, which supplies the lower portion of the greater curvature.

Understanding the lymphatic drainage can clarify the areas at risk for nodal involvement by cancer. The lymphatic drainage of the stomach is complex. Primary lymphatic drainage is along the celiac axis. Minor drainage occurs along the splenic hilum, suprapancreatic nodal groups, porta hepatis, and gastroduodenal areas. [10]

Once the second most common cancer worldwide, stomach cancer has dropped to sixth place, after cancers of the lung, breast, prostate, colon and rectum, and skin (non-melanoma). [5] Stomach cancer is the third most common cause of death from cancer. [5] The World Health Organization estimates that in 2018, gastric cancer accounted for 783,000 deaths worldwide. [1]

Tremendous geographic variation exists in the incidence of this disease around the world. Rates of the disease are low in Northern America and Northern Europe, and highest in Asian countries (eg, Mongolia, Japan, the Republic of Korea). The highest death rates are recorded in western Asian countries (Iran, Turkmenistan, Kyrgyzstan). [5]

Using data from 92 cancer registries in 34 countries representing 10 world regions, Arnold et al predicted that overall gastric cancer incidence rates will continue falling in most countries, including high-incidence countries such as Japan as well as low-incidence ones such as Australia. By 2035, incidence rates in 16 of those 34 countries will fall below the rare disease threshold (defined as 6 per 100,000 person-years). [11]

Nevertheless, the absolute number of new gastric cancer cases is expected to increase in the majority of countries. New cases could double in Canada, Cyprus, South Korea, Slovakia, and Thailand, while dropping slightly in a few other countries (eg, Bulgaria, Lithuania). [11]

While decreasing or stable incidence rates were consistently observed in people aged 50 years and above, Arnold et al predicted increases in incidence in those younger than 50 years in 15 of 34 countries, including Belarus, Chile, the Netherlands, Canada, and the United Kingdom. [11]

In the United States, gastric cancer represents 1.5% of all new cancer cases but 1.8% of cancer deaths. The overall 5-year relative survival rate, which was 14.3% in 1975, rose to 31.0% by 2008-2014. [2] The 5-year observed survival rate for surgically treated gastric cancer ranges from 94% for patients with stage IA disease to 82% for stage IIA, 54% for stage IIIA, to 18% for stage IIIC. [12]

The rates of gastric cancer are higher in Asian and South American countries than in the United States; in Japan, for example, stomach cancer is the most common cancer site in males. [5] Japan, Chile, and Venezuela have developed a very rigorous early screening program that detects patients with early-stage disease (ie, low tumor burden). These

patients appear to do quite well. In fact, in many Asian studies, patients with resected stage II and III disease tend to have better outcomes than similarly staged patients treated in Western countries. Some researchers suggest that this reflects a fundamental biologic difference in the disease as it manifests in Western countries.

In the United States, the incidence of stomach cancer in males is highest in blacks, followed by Asians and Pacific Islanders, Hispanics, and American Indian/Alaska natives. In females, rates are highest in Asians and Pacific Islanders, followed by blacks and Hispanics and American Indian/Alaska natives. In both males and females, rates are lowest in whites. [2]

In the United States, gastric cancer affects slightly more men than women; the American Cancer Society estimated that in 2020, 16,980 new cases would be diagnosed in men and 10,620 in women. [10] Worldwide, however, gastric cancer rates are about twice as high in men as in women. [5]

The median age at gastric cancer diagnosis in the United States is 68 years; fewer than 2% of cases occur in persons younger than 35 years. [2] The gastric cancers that occur in younger patients may represent a more aggressive variant or may suggest a genetic predisposition to development of the disease. Unfortunately, only a minority of patients with gastric cancer who undergo a surgical resection will be cured of their disease. Most patients have a recurrence.

Several studies have investigated the patterns of failure after surgical resection alone. Studies that depend solely on the physical examination, laboratory studies, and imaging studies may overestimate the percentage of patients with distant failure and underestimate the incidence of local failure, which is more difficult to detect.

A reoperation series from the University of Minnesota may offer a more accurate understanding of the biology of the disease. In this series of patients, researchers surgically reexplored patients 6 months after the initial surgery and meticulously recorded the patterns of disease spread. The total local-regional failure rate approached 67%. The gastric bed was the site of failure in 54% of these cases, and the regional lymph nodes were the site of failure in 42%. Approximately 26% of patients had evidence of distant failure. The patterns of failure included local tumor regrowth, tumor bed recurrences, regional lymph node failures, and distant failures (ie, hematogenous failures and peritoneal spread). Primary tumors involving the gastroesophageal junction tended to fail in the liver and the lungs. Lesions involving the esophagus failed in the liver. [13]

Gastric cancer has been one of the leading causes of cancer-related mortality over the past century. Today it is the 4th most common cancer in the world. Surgery

remains the only major curative option. Majority of these cancers are found to be unresectable on laparotomy. Most gastric cancer patients are diagnosed with advanced disease with the development of distant metastases hence assessment of prognostic markers in these patients should be done. Hence based on above condition the present study was planned for Clinico Pathological Assessment of Gastric Cancer in Bihar Region.

Methodology:

The present study was planned in Department of Pathology, Indira Gandhi Institute of Medical Science, Patna, Bihar, India. The present study was planned from duration of June 2018 to December 2018. In the present study 50 cases of adenocarcinoma of stomach were enrolled and evaluated. The patients were diagnosed on clinical, radiological, endoscopic examination with confirmation by histopathological examination of either endoscopic biopsy or the resected specimen. The resected gastrectomy specimens were examined grossly and tumour location, tumour dimensions, extent of tumour invasion, metastasis to lymph nodes, number of lymph nodes involved, abnormality in surrounding mucosa were recorded.

Clinicopathological parameters, including age, gender, and histological classification was retrieved from the medical records. For prospective study, gastrectomy (total/subtotal) and gastric biopsy specimens were received in 10% buffered formalin while for retrospective study, the slides and paraffin blocks were retrieved from the department of Pathology. Sections (4 µm thick) were de-paraffinized in xylene and hydrated through a graded series of ethanol. Sections were examined using routine Haematoxylin and eosin stain

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: Presenting with ulcers, abnormal growths, precancerous conditions.

Exclusion Criteria: Inadequate biopsy in terms of no glands, only fibro collagenous tissue.

Results & Discussion:

Gastric cancer is the 4th most commonly diagnosed cancer and the 2nd most common cause of cancer related deaths¹ The overall 5 year survival rate of patients with resectable cancer is around 10-30 %. ² Proximal stomach involvement is more common in western countries and is associated with more aggressive clinical course and a poorer prognosis. [14] In Asian countries, the intestinal subtype of adenocarcinoma is the commonest subtype.

[15] Surgical resection is the mainstay of treatment in early stage gastric cancer. However, most patients are diagnosed when the tumor is at an unresectable stage for which chemotherapy becomes the sole treatment option. The survival rate of patients with advanced carcinomas remains poor despite perioperative chemotherapy [16] or chemoradiation. [17]

Lauren has classified gastric cancer into diffuse and intestinal type that are different in regard to epidemiology, etiology, pathogenesis and behaviour. [18] Cadherin is a superfamily of calcium-mediated membrane glycoproteins. They binds to cytosolic proteins namely α -catenin, β -catenin, and, γ -catenin which in turn are linked to the actins to form the intracytoskeleton. [19] The cadherins are responsible for the homotypic cell-cell adhesion, Therefore, these play an important role in carcinogenesis and metastasis. E-Cadherin is expressed in all epithelial cell types. Underexpression of the E-Cadherin is found in gastric, hepatocellular, oesophageal, breast, prostatic, bladder and gynaecological carcinomas and correlates with infiltrative and metastatic ability. [20]

Table 1: Basic Details

Parameters	No. of Cases
Age:	
21 – 30 years	1
31 – 40 years	2
41 – 50 years	5
51 – 60 years	15
61 & above years	27
Sex:	
Males	37
Females	13
Total	50

Table 2: Sign & Symptoms

Sign & Symptoms	Observed in No. of Cases
Pain in Abdomen	50
Weight Loss	43
Nausea & Vomiting	41
Anorexia	36
Anaemia	28
Early Satiety	27
Mass	19
Dysphagia	8
Malena	2

Table 3: Site of Lesion and Histopathological Types

Site of Lesion	No. of Cases
Antrum	24
Fundus	2
Cardia	3
Greater Curvature	4
Lesser Curvature	8
Pylorus	9
Total	50
Histopathological Types	
Intestinal	31
Diffuse	17
Mixed	2
Total	50

Worldwide, the site of gastric cancer is changing in the western world. Incidence of distal gastric cancer is decreasing, and proximal gastric cancer is increasing (41% and 50% respectively) [21-22] Recent study from Kerala in India showed that though the predominant site of cancer was the antral mucosa, there was a trend towards proximal shift. Qurieshi et al showed that in the Kashmiri population, incidences of cancer in proximal, mid and distal stomach were 42%, 6.2% and 45.7% respectively. [24] Afridi et al reported growth at the cardiac end in 33%, pylorus and antrum in 40%, linitis plastica in 13.3% and only body and body and pylorus in 6.7% of the patients. [24]

Kim et al [25] reported that 80.3% young patients presented with advanced gastric carcinoma. In a Middle Eastern study, two-thirds of the patients presented with advanced gastric cancer. But in another study, early gastric cancer is more common in young age group than their older counterpart (19.7% vs 13.8%).

Study by McKenna and Appelman had 13 cases have observed 50% correlation between erosion and its histopathological diagnosis. [26] Levy N et.al., and Calabrese C et al have shown variation in results. [27-28] This variation could be due to the study conducted on different population, misinterpretation during endoscopic biopsy, misinterpretation by histopathologist, sampling error during the biopsy between the actual site biopsied and the endoscopic abnormality. All these studies suggest that the diagnosis of ulcer or gastritis is based on histopathological examination of gastric mucosa. [29-30]

Histopathological study of biopsy specimens are used to confirm endoscopic diagnosis in suspected malignancy or to rule out endoscopically benign appearing lesion. The endoscopic biopsies are performed not only for the diagnosis of the disease but also for monitoring the course, determining the extent of a disease, as responses to therapy and for the early detection of complications. [31]

The only potential curative therapy is surgical resection. For effective curative treatment, there must be complete resection of all gross disease with no residual microscopic disease. Accurate preoperative staging of gastric cancer is important in planning most effective therapy towards cure or palliation. [32] The depth of intramural tumour invasion and spreading beyond the gastric wall, the involvement of lymph nodes and distant metastases are the most important prognostic factors in gastric cancer. [33] Most patients present with advanced disease at diagnosis, so they could not be considered suitable for resection. In these patients, it is relevant to have a sensitive imaging tool for detection and thus avoid the morbidity of an unnecessary laparotomy. [34] "Imaging techniques" have assumed greater clinical value in the further assessment of an endoscopically or radiologically verified neoplastic

lesion of the stomach through the ability to evaluate its extent of invasion, metastatic involvement of lymph nodes and/or distant organs. [35] Because the aim of gastric cancer surgery is to excise the primary lesion adequately, it is very important to know the location of this lesion and the tumour margin before any therapeutic decision can be taken.

These findings emphasise and recommend endoscopy examination and endoscopic biopsy, endoscopy examination is incomplete without biopsy and histopathology as gold standard diagnostic procedure among patients suspected for gastric carcinoma. Endoscopic biopsy and histopathological correlation eliminates the necessity for diagnostic laparotomy. In our study, major number of carcinoma cases showed grossly ulcerating-fungating growth followed by ulceroproliferative growth, friable growth and nodular ulceration respectively.

Conclusion:

Gastric cancer is second most common cancer in male and fifth most common amongst females in East and Central Asia. The incidence of gastric cancer is twice as much in men as in women. Majority of cases had history of tobacco consumption, which clearly indicates the role of tobacco in causation of stomach cancer. Weak relation was seen in alcohol consumption. Screening of asymptomatic people in a high risk area may be useful in early detection of disease. Efforts to detect cancer early in developing countries would go a long way in reducing the disease burden and improving the outcome.

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