

Pathobiological characteristics of intestinal and diffuse-type of gastric carcinoma- retrospective study of gastric cancers

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ABSTRACT

Background: Gastric carcinomas have various pathological features. Based on patterns of growth and invasiveness, however, they fall into two types: diffuse type and intestinal type. These two types of carcinoma appear to be different in their histogenetic origins.

Objectives: To analyse various types of gastric cancer reported in last five years. To compare the features of intestinal and diffuse type gastric carcinoma including gross appearance, staging, grading of tumor.

Materials and Methods: This was a retrospective study of 324 gastric cancer which were surgically resected and received over 5 years. The tumors were divided into groups according to their gross and microscopic patterns. Gross appearance was classified based on Borrmann classification. Microscopic features evaluated include tumor cell type, extent of invasion, degree of maturation, formation of glandular structures, nodal metastasis.

Results: Totally 320 cases of gastric cancer were received of which 218(68%) were male, 102(32%) were female. Gastric cancers are rare below the age of 30 years. Comparing the type of gastric cancer intestinal type were 269(84%), diffuse type were 24(7.5%) and other type of gastric cancer including GIST, lymphoma, mucinous adenocarcinoma were 27(8.5%). Younger patients have higher stage of lymph node metastasis in diffuse type, but not for the intestinal type.

Conclusion: Gastric cancer more common in male (M:F= 2:1) and most frequently seen in 5th decade. Intestinal type constitutes the most common type of gastric tumor. Gross appearance of diffuse type was predominantly infiltrative (79%).

Key Words: Gastric cancer, diffuse type, intestinal type, gross appearance, grading, nodal metastasis

Introduction

Gastric carcinoma is a malignant epithelial tumour of the stomach mucosa with glandular differentiation. Its aetiology is multifactorial. [1] Gastric cancer is the second most common cancer worldwide, and despite decreasing mortality and incidence rates, it remains a leading cause of cancer-related deaths. Overall, gastric cancer rates are higher in developing countries and in lower socioeconomic groups. [2] Most populations show a 2-1 male to female ratio for gastric cancer cases. [3] Several studies have shown H. pylori infection to significantly increase the risk of both intestinal and diffuse types of gastric carcinomas, and it is now recognized as an established cause of gastric cancer. [2]

The histologic classification of Laurén's divides gastric adenocarcinoma into two main

types: intestinal and diffuse. Intestinal-type tumors are strongly associated with chronic gastritis and intestinal metaplasia. [4] Advanced gastric cancers of the intestinal type commonly appear as polypoid, fungating masses with surface ulceration. In contrast, diffuse-type cancers may appear as infiltrating or depressed cancers with no obvious mass present in the mucosa. [2] The intestinal type is characterized by cohesive cells which form gland-like structures, while for the diffuse type, tumor cells lack cell-to-cell interactions and infiltrate the stroma as single cell or small subgroups, leading to a population of non-cohesive, scattered tumor cell. [5]

Intestinal-type gastric carcinomas with a more favourable prognosis frequently show high levels of proliferation and apoptosis. Lauren's

classification thus proved pathologically relevant for the clinical treatment of gastric carcinomas. [6] The best predictor of prognosis is the pathologic stage, which includes the depth of invasion, the extent of nodal involvement, and the presence or absence of distant metastasis. [2] Younger patients had a higher incidence of lymph node metastasis of gastric cancer of diffuse type, but not for the intestinal type. [7] This study is done to compare the two different type of gastric cancer intestinal and diffuse with varying prognosis and to analyze gross appearance, stage and grade of the tumor.

Material and methods

The was a retrospective study of gastric cancer reported in gastrectomy specimen received in the Institute of pathology, Madras Medical College over a period of 5 years. The patients who were included in this study were screened with predetermined inclusion and exclusion criteria. All the cases reported as gastric malignancies by histopathology from gastrectomy specimen were

included irrespective of age and those with poor clinical data were excluded from the study.

324 gastric cancers were surgically resected and received over 5 years. H&E sections reviewed and microphotographs were taken. The tumors were divided into groups according to their gross and microscopic patterns. Gross appearance of advanced gastric cancer was classified based on Borrmann classification, which includes four types namely-Type I -Polypoid, Type II-Fungating, Type III-Ulcerated and Type IV-Infiltrative. Microscopic features evaluated include tumor cell type, extent of invasion, degree of maturation, formation of glandular structures, nodal metastasis. Immunohistochemistry record checked wherever needed. Intestinal type of gastric cancers was graded into well, moderate, poorly differentiated types based on formation of glands. [1] Staging of both intestinal and diffuse type of gastric cancer was done based on TNM classification (7th edition). [8]

TNM staging of gastric cancer

T category definitions, gastric cancer

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria
T1	Tumor invades lamina propria, muscularis mucosae, or submucosa
T1a	Tumor invades lamina propria or muscularis mucosae
T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures. T3 tumors also include those extending into the gastrocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures
T4	Tumor invades serosa (visceral peritoneum) or adjacent structures
T4a	Tumor invades serosa (visceral peritoneum)
T4b	Tumor invades adjacent structures such as spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum

N category definitions, gastric cancer

NX	Regional lymph node(s) cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 2 regional lymph nodes
N2	Metastasis in 3 to 6 regional lymph nodes
N3	Metastasis in 7 or more regional lymph nodes

Positive peritoneal cytology is classified as metastatic disease (M1)

Grading of intestinal type of gastric cancer

- Well differentiated: An adenocarcinoma with well-formed glands, often resembling metaplastic intestinal epithelium.
- Moderately differentiated: An adenocarcinoma intermediate between well differentiated and poorly differentiated.
- Poorly differentiated: An adenocarcinoma composed of highly irregular glands that are recognized with difficulty, or single cells that remain isolated or are arranged in small or large clusters with mucin secretions or acinar structures.

Results

Totally 324 cases of gastric cancer were received. Out of these 220 (68%) were male and 104 (32%) were female. Common in 51 to 60 years (35%). Intestinal type (83%) constitutes the most common type of gastric tumor. Diffuse type (10%) of gastric cancer was the next common type. (Table: 1) Other tumors reported include, Mucinous carcinoma, Lymphoma, Gastrointestinal stromal tumor. Rarely reported tumors includes, Undifferentiated carcinoma, Neuro endocrine carcinoma and Squamous cell carcinoma. Gross appearance predominantly was infiltrative (79%) in diffuse type and ulcerative (60%) in intestinal type. (Table: 2) T3 tumor staging was predominant in both diffuse and intestinal type of gastric cancer. (Table: 3) Most of the tumor reported as intestinal type was moderately differentiated. (Table: 4) There was no difference in stage of nodal metastasis in age ≤60 and >60 in intestinal type. Fig. 5,6) Younger patients (<60 years) presented with higher stage

of lymph node metastasis of gastric cancer of diffuse type (Fig. 7,8)

Table 1: Types of gastric cancer

Tumor type	Total	Percentage
Intestinal	268	82.72%
Diffuse	33	10.19%
Mucinous carcinoma	7	2.16%
Lymphoma	6	1.85%
Gastrointestinal stromal tumor	6	1.85%
Undifferentiated carcinoma	1	0.31%
Neuro endocrine carcinoma	1	0.31%
Squamous cell carcinoma	1	0.31%
Papillary type	1	0.31%

Table 2: Gross types of intestinal and diffuse gastric cancer

Gross type	Intestinal type	Diffuse type
Type i - polypoidal	7 (2.61%)	0
Type ii- fungating	100 (37.31%)	7(21.21%)
Type iii- ulcerated	161 (60.08%)	0
Type iv- infiltrative	0	26(78.79%)

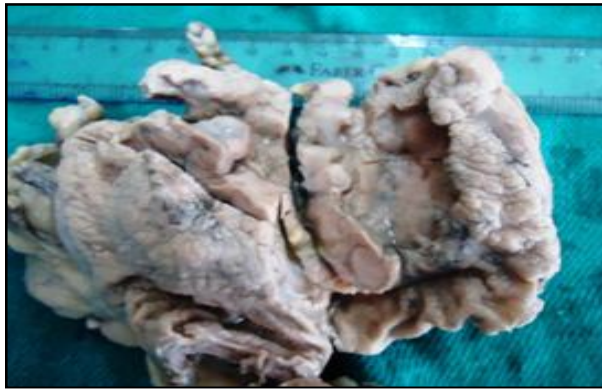


Fig. 1 Type II- Fungating mass in subtotal gastrectomy specimen



Fig. 2 Type IV- Infiltrative mass in total gastrectomy specimen

Table 4: Grading of intestinal type of gastric cancer

Tumor grading	Number of cases
Well differentiated	29(11%)
Moderately differentiated	153(57%)
Poorly differentiated	86(32%)

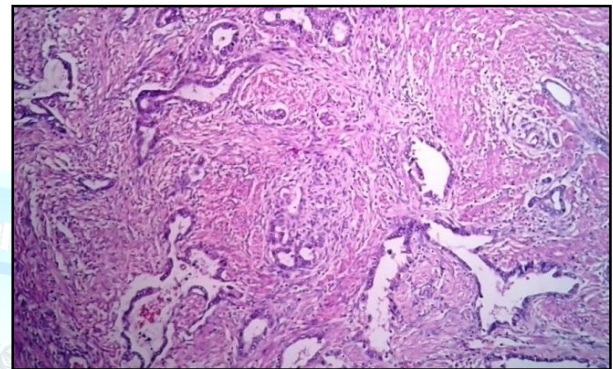


Fig. 3 H&E (10X)- Intestinal type of gastric cancer (moderately differentiated)

Table 3: TNM stage of gastric cancer

TNM staging	Intestinal type	Diffuse type
T1	13	0
T2	48	2
T3	194	23
T4	13	8
N0	95	10
N1	53	14
N2	60	5
N3	30	4
M0	268	33

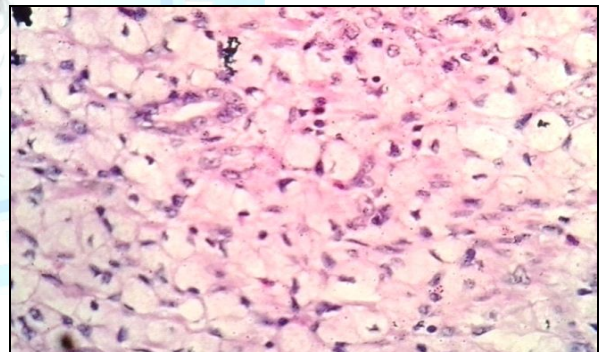


Fig. 4 H&E(45X)- Diffuse type of gastric cancer

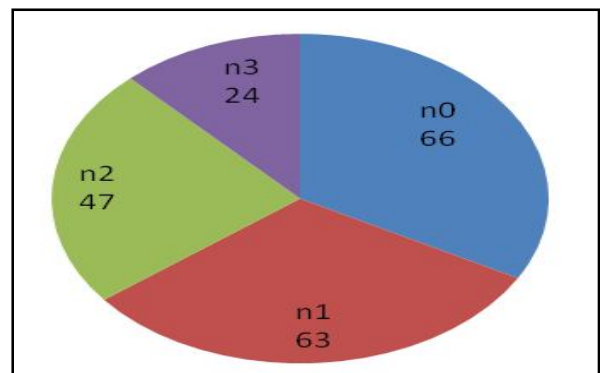


Fig.5 Nodal metastasis in intestinal type - analyzed in age ≤60

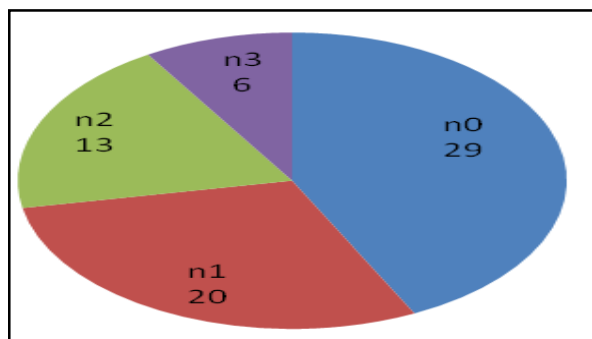


Fig.6 Nodal metastasis in intestinal type - analyzed in age>60

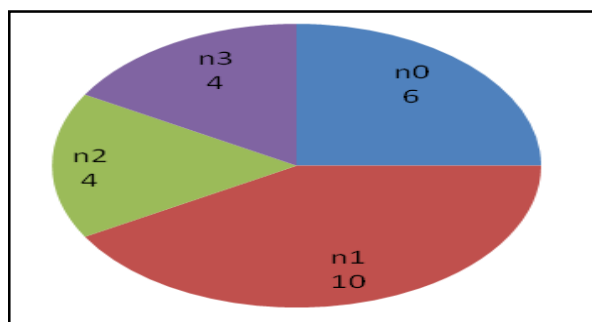


Fig.7 Nodal metastasis in diffuse type - analyzed in age ≤60

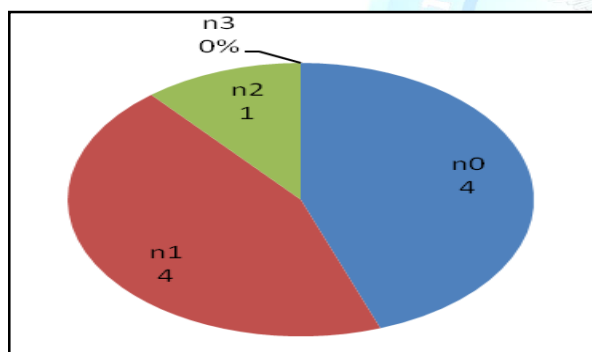


Fig.8 Nodal metastasis in diffuse type - analyzed in age >60

Adenocarcinoma is the most common malignant tumor of the stomach. The disease is extremely rare in children and adolescents. The depth of invasion and the extent of nodal and distant metastasis at the time of diagnosis remain the most powerful prognostic indicators for gastric cancer.^[9]

In the present study gastric cancer is more in 5th decade and in males (M:F- 2:1). Gastric cancer is rare in age less than 30 years (5%). Intestinal type was the most type of gastric cancer (83%). Gross appearance of diffuse and intestinal type were compared based on Borrmann classification, which indicates infiltrative type common in diffuse type and ulcerative type common in intestinal type. Nodal metastasis was examined in all the gastric cancer. The results were compared by different histological type (diffuse type, Intestinal type) as well as different age groups (age ≤ 60 and age >60 years). This shows that Younger patients had a higher incidence of lymph node metastasis of gastric cancer of diffuse type, but not for the intestinal type. Results of the present study was in accordance with other studies,^[6,10,11] gastric cancer was most common in 5th to 6th decade. Male: female ratio was 2:1. Intestinal type of gastric cancer was most common when compared with diffuse type. Gastric cancer was most common in 5th decade and Male: female ratio is 2:1. Gross appearance of diffuse type was predominantly infiltrative type. T3 tumor staging was most frequent in both diffuse and intestinal type. Younger patients (<60 years) had higher stage of nodal metastasis in diffuse type.

Discussion

Table 5: Results of the present study compared with other studies

Study	Age	Male	Female	M:f ratio	Intestinal type	Diffuse type	Others
Present study	51-60	220(68%)	104(32)	2:1	268(83%)	33(10%)	23(7%)
Ming SC et al ^[10]	>50	104(61%)	67(39%)	2:1	114(67%)	57(33%)	-
Zheng H et al ^[6]	60-70	222(70%)	94(30%)	2:1	-	-	-
Graziosi L et al ^[11]	50-60	68(60%)	45(40%)	2:1	65(57%)	45(39%)	4(4%)

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