

## Original research article

**The Correlation Between The Clinico- Pathological Factors And Gastric Cancer: A Retrospective Study.****Dr. Vandana<sup>1</sup>, Dr.Kannu Priya<sup>2</sup>, Dr. Pallavi Mehra<sup>3</sup>, Dr.N.K.Bariar<sup>4</sup>****<sup>1</sup>PG Student, Department of Pathology, Patna Medical College and Hospital, Patna, Bihar, India.****<sup>2</sup>Senior Resident, Department of Pathology, Patna Medical College and Hospital, Patna, Bihar, India.****<sup>3</sup>Assistant Professor, Department of Pathology, Patna Medical College and Hospital, Patna, Bihar, India.****<sup>4</sup>HOD, Department of Pathology, Patna Medical College and Hospital, Patna, Bihar, India.****Corresponding Author: Dr. Vandana****Abstract****Aim:** to find correlation between clinical and pathological factors of gastric cancer.**Material and Methods:** This retrospective study was carried out in the Department of Pathology, Patna Medical College and Hospital Patna, Bihar, India from December 2017 to July 2018. Total 600 patients were included in this study.**Results:** Of these 600 patients, 370 (61.67%) underwent distal gastrectomy, 24 (4%) proximal gastrectomy via abdomen and 145 (24.17%) via thorax, and 61 (10.16%) underwent total gastrectomy. Distal and total gastrectomy had more numbers of clearances of lymph nodes than the other operational approaches. The postoperative complications occurred in 51 patients 51/600, 8.5%.The overall mortality was 0.66% (4/600).The diameter of the neoplasm was positively correlated with the depth of infiltration and lymphatic metastasis rate while hemoglobin was the opposite. 92 (15.33%) of 600 were early gastric carcinoma (EGC) with metastasis of lymph nodes in 12 patients (12/92, 13.04%).**Conclusion:** This retrospective study has shown that clinicopathological characters in gastric cancer varied with sex, location, and diameter of the tumor.**Keywords:** gastric cancer, gender, location, size**Introduction**

Gastric cancer is a heterogeneous, multifactorial disease, which is known as the fifth most common cancer and the third leading cause of cancer-related death worldwide in 2018.<sup>1 2</sup> According to previous reports, ~0.7million people died because of gastric cancer each year,<sup>3</sup> and about 70% of the gastric cancer cases had high fatality, significantly higher than other cancers such as the liver and breast cancers.<sup>4</sup> However, the incidence and mortality of gastric carcinoma vary geographically; they were dramatically different between Western and Eastern countries.<sup>3</sup>

The epidemiological and clinicopathological characteristics of gastric cancer still largely remain uncertain, although some risk factors have been identified in the study. It has been reported that the survival rates were lower among smokers, alcohol drinkers, obesity and people who have the symptom of esophageal acid reflux and consume pickled, salty and smoked food.<sup>5-6</sup> Studies also suggested that the incidence rate of gastric cancer was highly correlated with age, especially among patients aged between 50 and 70 years old.<sup>7-8</sup> It has

been reported that gastric carcinoma is one of the heaviest burdens of cancer-related cost, the absolute numbers of gastric cancer cases and the prognosis remain big issues in the health programmes.<sup>9</sup>

The current most popular therapy for gastric cancer is surgery combined with chemotherapy. Surgery is the most preferred treatment for gastric carcinoma, but the survival rate of patients undergoing surgery remains very low. Previous studies have revealed that the average survival time of patients with advanced gastric cancer is <12 months<sup>10,11</sup>. Therefore, how to timely assess the condition, judge the prognosis risk after therapy and develop a reasonable postoperative care programme becomes a vital part of gastric cancer treatment.<sup>12,13</sup> Many clinico-pathological factors, including clinical stage, tumour size, infiltration depth, Lauren classification and lymph node metastasis rate, might jointly influence the prognosis in patients with gastric carcinoma.<sup>14,15</sup> It is important but challenging to identify the most significant and independent factors associated with prognosis since many factors are highly correlated. To have a systematic comprehension of gastric carcinoma and to identify independent risk factors on gastric cancer patients, we conducted the current study.

### Material and methods

This retrospective study was carried out in the Department of Pathology, Patna Medical College and Hospital Patna, Bihar, India from December 2017 to July 2018, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent detailed history was taken from the 600 patient or the relatives if the patient was not in good condition.

### Methodology

We analyzed the following clinicopathologic and surgical factors:

age, sex, hemoglobin, operation manners, operation time, and amount of transfusion during operation, postoperative hospital stay, postoperative complications, positive proximal margin, location of tumor, tumor size, differentiation, depth of tumor invasion, lymph nodes and lymphatic metastasis rate.

Frequency of positive lymph nodes = numbers of metastatic lymph nodes / all lymph nodes excised  $\times 100\%$ .

### Statistical analysis

The recorded data was compiled entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations. Test applied for analysis was t-test. The confidence interval and p-value were set at 95% and 5%.

### Results

**Table 1: Comparison of operation manner with numbers of lymph nodes, time for operation, amount of blood transfusion during operation, hospitalization days and complications ( $\bar{x} \pm s_x$ )**

Manners of operation	N(600)	Numbers lymph nodes	Time for operation (hours)	Amount of blood transfusion (mL)	Hospitalization stays (days)	Complication (%)
Distal gastrectomy	370	10.4 $\pm$ 0.2*	3.1 $\pm$ 0.02	406.3 $\pm$ 14.7*	15.4 $\pm$ 0.9	8.8

Proximal gastrectomy via abdomen	24	8.4 ± 0.3	4.1 ± 0.1*	616.4 ± 41.1*	17.6 ± 1.7	16*
Proximal gastrectomy via thorax	145	8.1 ± 0.1	3.1 ± 0.01	755.1 ± 18.3	14.8 ± 0.8	1.3
Total gastrectomy	61	12.6 ± 0.4*	4.2 ± 0.2*	742.2 ± 44.9	18.6 ± 1.5	11.6
<i>p-value</i>		<0.0001	<0.0001	<0.0001	>0.05	<0.001

\*Compared with other operative approaches

**Table 2: Comparison of depth of infiltration with age, diameter, hemoglobin, and lymphatic metastasis rate ( $\bar{x} \pm s_x$ )**

Depth of invasion	N (600)	Age (yrs)	Diameter (cm)	Hemoglobin(g / L)	Lymphatic metastasis rate (%)
pT1(m)	63	50.7 ± 1.1	2.1 ± 0.3	12.3 ± 0.4	3.1 ± 0.6
pT1(ms)	33	54.9 ± 1.4*	2.4 ± 0.5	11.6 ± 0.5*	4.0 ± 1.1
pT2	37	55.7 ± 1.3*	2.9 ± 0.4	11.5 ± 0.2*	8.9 ± 1.4*
pT3	42	56.4 ± 1.2*	4.1 ± 0.4*	11.7 ± 0.2*	18.1 ± 2.6*
pT4	425	57.1 ± 0.2*	5.1 ± 0.2*	11.4 ± 0.2*	34.7 ± 1.3*
<i>p-value</i>		<0.003	<0.0001	<0.001	<0.0001

Compared with pT1 (m).

**Table 3: Comparison of differentiation with age, diameter, hemoglobin and lymphatic metastasis rate ( $\bar{x} \pm s_x$ )**

Differentiation	N (600)	Age (yrs)	Diameter (cm)	Hemoglobin (g / L)	Lymphatic metastasis rate (%)
I	49	60.2 ± 1.2	3.3 ± 0.3	10.9 ± 0.5	10.1 ± 3.1*
II	91	58.1 ± 0.6	3.9 ± 0.4	11.4 ± 0.2	24.4 ± 2.1
III	145	58.8 ± 0.4	4.1 ± 0.1	11.1 ± 0.4	20.9 ± 1.6
IV	315	52.7 ± 0.2*	4.7 ± 0.1*	11.6 ± 0.1*	30.9 ± 1.1*
<i>p-value</i>		< 0.0001	= 0.003	= 0.01	< 0.0001

\*Compared with other groups

**Table 4: Comparison of tumor site with age, diameter, hemoglobin and positive lymph node rate ( $\bar{x} \pm s_x$ )**

Location of tumor	N (600)	Age (yrs)	Diameter (cm)	Hemoglobin (g / L)	Lymphatic metastasis rate (%)
Pylorus	19	52.7 ± 2.6	3.6 ± 0.5	12.3 ± 0.9	13.6 ± 3.1
Antrum	192	55.8 ± 0.3*	4.8 ± 0.3	12.1 ± 0.4	25.8 ± 1.3
Incisura	181	54.8 ± 0.3	3.0 ± 0.2	12.1 ± 0.1	20.9 ± 1.6
Corpus	39	55.7 ± 1.3	5.9 ± 0.4*	11.5 ± 0.2	35.8 ± 3.9*
Fundus	169	58.2 ± 0.4*	5.1 ± 0.3*	12.6 ± 0.1	33.4 ± 1.6*
<i>p-value</i>		< 0.0001	< 0.0001	> 0.005	< 0.001

\*Compared with other locations.

**Table 5: Comparison of sex with tumor location, differentiation, depth of invasion and positive lymph node rate ( $\bar{x} \pm s_x$ )**

Gender	Location (%)			Differentiation (%)			Depth of invasion (%)			Frequency of metastatic lymph node (%)	
	Proximal	Middle	Distal	Well	Middle	bad	pT1	pT2	pT3	<35	>35
Male	35	21	44	20	24	56	12	7	81	66	34
Female	51	9	40	12	18	70	12	8	80	59	41
		<0.001	<0.001					>0.05	=0.01	<0.001	

**Table 6: Multi-factors analysis of lymphatic metastasis in gastric patients**

Related factors	Regression coefficient	Standard error	Standard regression coefficient	P
Constant	-22.4	7.3		0.001
Age	-0.006131	0.071	-0.20	0.431
Sex	-6.466	2.029	-0.088	0.001
Tumor location	2.297	0.699	0.081	0.002
Diameter of tumor	2.379	0.479	0.151	0.0001
Depth of invasion	7.031	0.799	0.291	0.0001
Differentiation	3.699	1.133	0.089	0.001

## Discussion

Gastric cancer remains one of most common causes of death. Although the etiology of gastric cancer is still unclear, but studies have shown that many factors are associated with the development, metastasis of gastric cancer, and recurrence after operation.<sup>16-18</sup> Recent studies suggest that infection with *Helicobacter pylori* may play an important role in the development of gastric cancer.<sup>19,20</sup> It has been proposed that *Helicobacter pylori* infection may produce acute and chronic gastritis, intestinal metaplasia, dysplasia, and eventually resulting in gastric cancer. Some abnormal expression in gene is involved in carcinogenesis of gastric cancer such as matrix metalloproteinases gene, *p53* gene and dinucleotide repeat sequence gene. Abnormal contents of some trace elements may also be one of the risk factors in gastric cancer.<sup>21-24</sup>

Early gastric cancer (EGC) has been considered to be a form of gastric malignancy with a relatively good long-term prognosis compared to that of advanced gastric cancer because of rare metastasis in lymph nodes.<sup>25,26</sup> In Japan, EGC is diagnosed in 30%-50%, due to partly at least the extensive use of endoscopy and mass screening programs.<sup>27,28</sup> In this study, the proportion of EGC diagnosed in all patients is 92 (15.33%) similar to the proportion in the United States and Europe.<sup>29,30</sup> In recent years, endoscopic treatment has become increasingly popular as an alternative to surgical treatment of patients with EGA in hope of offering superior quality of life (QOL).<sup>31</sup> However, because of presence of metastasis in 10%-20% and skip metastasis of lymph nodes, whether the rationale for a standard resection with systematic lymphadenectomy is necessary is still a controversial issue.<sup>32</sup>

Different operative approaches were carried out according to the different locations of the tumor. In our study, the number of lymph nodes excised was the largest in total gastrectomy, followed by distal gastrectomy which may be related to the resection of all or most parts of omentum. The number of lymph nodes excised in proximal gastrectomy via a

transabdomen was similar to via transthorax. There was shorter time for operation and lower frequency of complication in proximal gastrectomy via transthorax while lower blood transfusion in proximal gastrectomy via transabdomen. The postoperative hospitalization stay and the positive resection margin were same between them. The complications varied among different operations: gastric retention was common in distal gastrectomy while thorax effusion and infection of lung were mainly found in total gastrectomy.

Although the overall incidence of gastric cancer has remained stable in the West, there is well- documented shift from distal to proximal lesion. The clinical relevance of this shift is that the overall prognosis for patients with proximal gastric cancer is worse than for those with distal tumor. This difference in survival may be attributed to a variety of factors, ranging from an increased biologic aggressiveness of proximal tumors to an advanced stage of presentation<sup>33,34</sup>. In study, a higher frequency of positive lymph nodes was found in gastric cancer located on corpus and the fundus which may be associated with the larger diameter of the tumor in corpus and the fundus. In tumors with larger diameters there were worse differentiation, deeper infiltration, and higher frequency of positive lymph nodes. Apparently, the prognosis will be worse in these patients. The present results also show that the more proximal lesions, bad differentiation, and the higher >35% frequency of positive lymph nodes can be found in female than in male. The numbers of metastatic lymph nodes play an important role in the long-term outcome after curative resection<sup>35,36</sup>. Thus it is suggested that extended lymphadenectomy should be performed in advanced gastric cancer<sup>37</sup>. Our multivariate analysis indicated that among six clinicopathologic variables (age, sex, location of tumor, tumor diameter, depth of invasion and differentiation), the depth of invasion was the most important factor influencing metastasis of lymph node.

### Conclusion

This retrospective study has shown that clinicopathological characters in gastric cancer varied with sex, location, and diameter of the tumor. The depth of invasion plays a very important role in metastasis of lymph node. The prognosis in female with gastric cancer may be worse than in man. Because metastasis of lymph nodes may occur even in patients with EGC, radical gastrectomy with lymphadenectomy may be necessary in all stages of gastric cancer.

### Reference

1. WHO. International agency for research on cancer, 2018.
2. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394–424.
3. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. *JCO* 2006;24:2137–50.
4. Guggenheim DE, Shah MA. Gastric cancer epidemiology and risk factors. *J Surg Oncol* 2013;107:230–6
5. Lindblad M, Rodríguez LAG, Lagergren J. Body mass, tobacco and alcohol and risk of esophageal, gastric cardia, and gastric non-cardia adenocarcinoma among men and women in a nested case-control study. *Cancer Causes Control* 2005;16:285–94.
6. Strumylaite L, Zickute J, Dudzevicius J, et al. Salt-preserved foods and risk of gastric cancer. *Medicina* 2006;42:164–70.
7. Karimi P, Islami F, Anandasabapathy S, et al. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. *Cancer Epidemiology Biomarkers & Prevention* 2014;23:700–13.
8. Howlader NJHscgc. Seer cancer statistics review, 1975-2008, 2011.

9. Bray F, Ferlay J, Soerjomataram I, et al. GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;2018.
10. Magalhães H, Fontes-Sousa M, Machado M. Immunotherapy in advanced gastric cancer: an overview of the emerging strategies. *Canadian Journal of Gastroenterology and Hepatology* 2018;2018:1–8.
11. Ajani JA. Is the addition of cisplatin to S-1 better than S-1 alone for patients with advanced gastroesophageal cancer? *Nat Clin Pract Oncol* 2008;5:508–9.
12. Penson DF. Re: variation in surgical-readmission rates and quality of hospital care. *J Urol* 2014;191:1363–4.
13. Lee K-G, Lee H-J, Yang J-Y, et al. Risk factors associated with complication following gastrectomy for gastric cancer: retrospective analysis of prospectively collected data based on the Clavien-Dindo system. *J Gastrointest Surg* 2014;18:1269–77.
14. Qiu M-zhen, Cai M-yan, Zhang D-sheng, et al. Clinicopathological characteristics and prognostic analysis of Lauren classification in gastric adenocarcinoma in China. *J Transl Med* 2013;11:58.
15. Smith DD, Schwarz RR, Schwarz RE. Impact of total lymph node count on staging and survival after gastrectomy for gastric cancer: data from a large US-population database. *JCO* 2005;23:7114–24.
16. Sun GY, Liu WW, Zhou ZQ, Fang DC, Men RP, Luo YH. Free radicals in development of experimental gastric carcinoma and precancerous lesions induced by N-methyl-N'-nitro-N-nitrosoguanidine in rats. *Huaren Xiaohua Zazhi*, 1998;6:219-221
17. Liu HF, Liu WW, Fang DC. Study of the relationship between apoptosis and proliferation in gastric carcinoma and its precancerous lesion. *Shijie Huaren Xiaohua Zazhi*, 1999;7:649-651
18. Xiong MM, Jiang JR, Liang WL, Meng XL, Zhang CL, Peng C. A study on vasoactive intestinal peptide in serum, carcinomatous tissue and its surrounding mucosa in patients with gastric cancer. *Huaren Xiaohua Zazhi*, 1998;6:121-122
19. He XX, Wang JL, Wu JL, Yuan SY, Ai L. Telomerase expression, Hp infection and gastric mucosal carcinogenesis. *Shijie Huaren Xiaohua Zazhi*, 2000;8:505-508
20. Zhang L, Jiang J, Pan KF, Liu WD, Ma JL, Zhou T, Perez-Perez GI, Blaser MJ, Chang YS, You WC. Infection of H.pylori with cagA+ strain in a high-risk area of gastric cancer. *Huaren Xiaohua Zazhi*, 1998;6:40-41
21. Li N, Xu CP, Song P, Fang DC, Yang SM, Meng RP. Overexpression of matrix metalloproteinases gene in human gastric carcinoma. *Huaren Xiaohua Zazhi*, 1998;6:118-120
22. Zhang QX, Dou YL, Shi XY, Ding Y. Expression of somatostatin mRNA in various differentiated types of gastric carcinoma. *World J Gastroenterol*, 1998;4:48-51
23. Lu HD, Wang ZQ, Pan YR, Zhou TS, Xu XZ, Ke TW. Comparison of serum Zn, Cu and Se contents between healthy people and patients in high, middle and low incidence areas of gastric cancer of Fujian Province. *World J Gastroenterol*, 1999;5:84-86
24. Cao GH, Yan SM, Yuan ZK, Wu L, Liu YF. A study of the relationship between trace element Mo and gastric cancer. *World J Gastroenterol*, 1998;4:55-56
25. Yu W, Whang I, Suh I, Averbach A, Chang D, Sugarbaker PH. Prospective randomized trial of early postoperative intraperitoneal chemotherapy as an adjuvant to resectable gastric cancer. *Ann Surg*, 1998;228:347-354
26. Isozaki H, Okajima K, Momura E, Ichinona T, Fujii K, Izumi N, Takeda Y. Postoperative evaluation of pylorus preserving gastrectomy for early gastric cancer. *Br J Surg*, 1996;83:266-269
27. Endo M, Habu H. Clinical studies of early gastric cancer. *Hepato Gastroenterology*, 1990;37:408-410

28. Sano T, Sasako M, Kinoshita T, Maruyama K. Recurrence of early gastric cancer: follow up of 1475 patients and review of the Japanese literature. *Cancer*, 1993;72:3174-3178
29. Hioki K, Nakane Y, Yamamoto M. Surgical strategy for early gastric cancer. *Br J Surg*, 1990;77:1330-1334
30. Mendes de Almeida JC, Bettencourt A, Costa CS, Mendes de Almeida JM. Curative surgery for gastric cancer: study of 166 consecutive patients. *World J Surg*, 1994;18:889-895
31. Takeshita K, Tani M, Inoue H, Saeki I, Hayashi S, Honda T, Kando F, Saito N, Endo M. Endoscopic treatment of early oesophageal or gastric cancer. *Gut*, 1997;40:123-127
32. Sowa M, Kato Y, Nishimura M, Kubo T, Maekawa H, Umeyama K. Surgical approach to early gastric cancer with lymph node metastasis. *World J Surg*, 1989;13:630-636
33. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA*, 1991; 265:1287-1289
34. Salvon-Harman JC, Cady B, Nikulasson S, Khettry U, Stone MD, Lavin P. Shifting proportions of gastric adenocarcinomas. *Arch Surg*, 1994;129:381-389
35. Yoo CH, Noh SH, Shin DW, Choi SH, Min JS. Recurrence following curative resection for gastric carcinoma. *Br J Surg*, 2000;87: 236-242
36. Tong ZM. Relationship between lymph node metastasis and postoperative survival in gastric cancer. *Huaren Xiaohua Zazhi*, 1998; 6:224-226
37. Siewert JR, Kestlmeier R, Busch R, Bottcher K, Roder JD, Muller J, Fellbaum C, Hfler H. Benefits of D2 lymph node dissection for patients with gastric cancer and pN0 and pN1 lymph node metastases. *Br J Surg*, 1996;83:1144-1147

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