



GASTRIC CANCER: A 5 YEAR RETROSPECTIVE ANALYSIS OF CLINICAL, PATHOLOGICAL AND TREATMENT ASPECTS FROM A TERTIARY CARE CENTER IN SOUTH INDIA.

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ABSTRACT

Context: Gastric cancer(GC) is fifth most common cancer worldwide. Mostly presents with advanced stage and poor overall survival.

Methods: Retrospective study on clinical, pathological, pattern of distant metastasis(DM) , treatment aspect of GC treated between January 2014 to December 2018 in a tertiary care center in south India.

Statistical analysis : Chi square test and multivariate analysis (MVA) were used for analysis. P <0.05 was considered significant.

Results: Median age at diagnosis is 57 years. Higher male : female ratio. Most common presentation was abdominal pain followed vomiting. Malignant Gastric outlet obstruction(MGOO) was present in 22.7%. Histologically , all patients had adenocarcinoma with predominantly moderate differentiation (51.1%). Liver (19.1%)was most common site of metastasis . Curative surgery was done in 35.5% of patients. D2 lymph node dissection was performed in 12.4% of patient. Patients were given perioperative /preoperative/ adjuvant / palliative chemotherapy. MVA revealed history of tobacco use, body of stomach tumor location, nodal disease were risk factors for DM.

Conclusion : The present analysis revealed use of tobacco, alcohol intake were main risk factors for GC. Most of the patients present in advanced stage , so prevention by avoiding risk factors and early detection by signs , symptoms and endoscopy are necessary. Use of tobacco, site of tumor location, nodal disease were factors associated with DM. Aggressive management with both surgery and chemotherapy is warranted for locally advanced disease.

KEYWORDS : gastric cancer, risk factors, distant metastasis.

INTRODUCTION

Gastric cancer(GC) is fifth most common cancer in world. The incidence of GC has been high in East Asian countries. In India GC stands 6th with 60,222 new cases about 4.5% with cumulative risk of 0.53^[1]. GC usually presents at advanced stage and 5 yrs overall survival is 20%^[2]. Survival rates are higher in countries which have screening programs that lead to early detection and where distal cancer predominates^[3]. Risk factors associated with GC are dietary habit, H.pylori infection, alcohol intake ,tobacco use and family history of malignancy^[4-6]. Treatment include multidisciplinary approach of surgery , perioperative / adjuvant chemotherapy with or without radiation. So understanding the epidemiology ,clinico-pathological, treatment modality of disease can help in awareness, prevention, early detection and effective treatment in order to improve survival. We conducted an institutional retrospective analysis to study the current epidemiological characteristics, metastatic pattern, and risk factors of distant metastasis (DM)in GC.

SUBJECTS AND METHODS:

The present study was a retrospective analytical study, conducted in a dedicated cancer centre in a tertiary care hospital in south India. The study population included, all histopathologically confirmed cases of GC treated between January 2014 and December 2018. The data was retrieved from the hospital cancer registry. All these patients were diagnosed on clinical, radiological and endoscopic examination. The cases with primary gastric lymphoma, gastro intestinal stromal tumours (GIST) and gastric

melanoma were excluded. Staging was performed according to AJCC staging system (7th edition) based on the available clinical and radiological findings. The compiled data included medical history of family history of GC, use of tobacco , consumption of alcohol, chief presenting complaints, histological grade, TNM staging and the site of metastasis. IBM SPSS statistics software for windows, version 25.0 (Armonk, NY: IBM Corp) was used for data analysis. The frequency distribution and association among different clinicopathological variables was evaluated by Chi-square analysis, and the risk factors of DM were evaluated by multivariate analysis (MVA).

RESULTS:

Base line parameters (Table 1)

This study included 225 patients with male : female 2.51:1. Median age of diagnosis was 57. Age distribution varied from 23 years to 87 years. Younger patients (≤ 40 years) constituted 12.4%. Frequency of use of tobacco were 44% and alcohol intake was 43.6%. Performance status of patients according to ECOG 1(50.7%) > 2(40.0%) > 3(8%) > 4(4%). Patients had comorbid conditions type II diabetes mellitus (20.4%), systemic hypertension (15.6%), coronary artery disease (5.3%). Most common symptom at presentation was abdominal pain in 85.8% patients with median duration of 3months ,followed by vomiting in 75.1% patients with medication duration of 1 month, 42.7% patient had weight loss. Most common sub-site of tumor location was body of stomach (26.6%) followed by pylorus (24.9) and antrum (24.4%). Most of the patients had moderately differentiated

adenocarcinoma (51.1%) followed by poorly differentiated adenocarcinoma (26.2%). Among T stage T3 was common with 49.3% followed by 4a(23.1%) and T2(16.3%) respectively. Majority had node positive disease (86.5%). Overall 99 patients (44%) had DM at presentation . Liver (19.1%) was most involved site followed by omentum (6.7%) and left supraclavicular node(6.7%).

Table 1 :Frequency distribution of different parameters among study population

Parameters	Number	Percentage %
Age		
Median	57	
Range	23-87	
Age group		
≤ 40	28	12.4
> 40	197	87.6
Sex		
Male	161	71.6
Female	64	28.4
Performance status (ECOG)		
1	114	50.7
2	90	40.0
3	18	8.0
4	1	4.0
Use of tobacco		
Yes	99	44.0
No	121	53.8
Unknown	5	5.0
Alcohol intake		
Yes	98	43.6
No	126	56.0
Unknown	1	0.4
Family history of malignancy		
Yes	24	10.7
No	199	88.4
unknown	2	0.9
Symptoms		
Abdominal pain	193	85.8
vomiting	169	75.1
Melena	47	20.9
Weight loss	96	42.7
Gastric outlet obstruction	51	22.7
Subsite of tumor		
Cardia	31	13.8
Fundus	4	1.8
Body	60	26.6
Lesser curvature	16	7.1
Antrum	55	24.4
Pylorus	56	24.9
Diffuse	2	0.9
Grade of adenocarcinoma		
I	35	15.6
II	115	51.1
III	59	26.2
Node		
Positive	195	86.5
Negative	24	10.7
Metastasis at presentation	99	44
Site of Distant metastasis		
Liver	43	19.1
Omentum	15	6.7
Left supra clavicular node	15	6.7
Peritoneum	13	5.8
Lung	2	0.9
Ovary	3	1.3
Adrenal	4	1.8
Scalp	1	0.4
Gall bladder	1	0.4

Management of patients(Table 3).

With respect to treatment 93 patients (41.3%) had curative treatment and 132 patients (58.7%) had palliative treatment. Patients underwent Total gastrectomy(5.8%), Subtotal gastrectomy(18.2%), Partial gastrectomy (1.3%), Distal gastrectomy(10.2%). D2 Lymph node dissection were done in 12.4% and D1 lymph node dissection were done in 23.1% of patients. Among chemotherapy given, 1.3% had perioperative chemotherapy, 5.4% had preopchemotherapy, 33.3% had adjuvant chemotherapy , 41. 3% had palliative chemotherapy. CDDP + 5 5FU regimen was commonly administered as adjuvant and palliative chemotherapy . On MVA the factors associated with DM were use of tobacco(p=0.020), site of tumor location(p=0.016) and node stage(0.000).(Table 3)

Table 2: Distribution of cases according to management

Treatment	Number	Percentage %
Intent of treatment		
Curative	93	41.3
Palliative	132	58.7
Surgery		
Toal gastrectomy	13	5.8
Subtotal gastrctomy	41	18.2
Partial gastrectomy'	3	1.3
Distal gastrectomy	23	10.2
Gastro jejunostomy	8	3.6
Feeding jejnoastomy	8	3.6
Lymphnode dissection		
D1 lymph node dissection	52	23.1
D2 lymph node dissection	28	12.4
Perioperative chemotherapy		
ECF	2	0.9
FLOT	1	0.4
Preoperative chemotherapy.		
CDDP + 5FU	8	3.6
Carboplatin and paclitaxel	4	1.8
Adjuvant chemotherapy		
CDDP+5FU +/- leucovorin	62	27.6
ECF	5	2.2
Carboplatin and paclitaxel	1	0.4
FOLFOX/CAPEOX	5	2.2
Weekly 5FU	2	0.9

CDDP- cisplatin
 5FU- 5flurouracil
 ECF- epirubicin + cisplatin + 5FU infusion
 FLOT- docetaxel + oxaliplatin + leucovorin + 5FU
 CAPEOX- capcetabine + oxaliplatin

Table 3: Risk factors for DM evaluated by multivariate analysis (95% level of significance)

Parameters	Metastases (%)	P value
Sex		
Male	42.9	
Female	46.9	0.213
Age group		
≤ 40	39.3	
> 40	44.7	0.984
ECOG		
1	40.4	
2	46.7	
3	61.1	
4	-	0.354
Use of tobacco		
yes	35.4	
No	50.4	0.020
Alcohol intake		
Yes	39.8	
no	47.6	0.242
Family history of malignancy		
Yes	45.8	
no	43.2	0.623

Signs and symptoms		
vomiting	45.0	0.697
Abdominal pain	43.5	0.909
Melaena	42.6	0.699
Gastric outlet obstruction	41.2	0.536
Weight loss	39.6	0.198
Sub-site of tumor		
Cardia	48.4	
Fundus	50.6	
Lesser curvature	37.5	
Body of stomach	61.0	
Antrum	40.0	
Pylorus	28.6	
Linitis plastica	100	0.016
Grade of adeno carcinoma		
I	42.9	
II	41.7	
III	52.5	0.420
T stage		
0	-	
1	-	
2	34.2	
3	45.9	
4α	48.1	
4b	45.5	0.179
N stage		
0	-	
1	17.5	
2	55.4	
3	57.6	0.000

T: tumor

N: node

ECOG: Eastern cooperative oncology group

DISCUSSION

The incidence of GC varies worldwide, higher incidence found in south east Asia. The aetiology of GC is multi-factorial. Dietary factors attributed are salt rich and smoked foods. Conversely, diets high in raw vegetables, fresh fruits are associated with decreased risk^[4-6]. Globally tobacco smoking has been indicated as the risk factor for GC in case-control and cohort studies^[8]. Different forms of tobacco used are hukka, snuff, bidis and cigarettes^[7]. Smoking tobacco has been found to be an independent risk factor for GC^[9]. Alcohol is carcinogenic to the esophagus and cardia cancers but not to distal GC^[10]. The most important risk factor for GC is observed to be the infection with *H. pylori*^[11]. Polymorphism in genes involved in inflammation are involved in development of GC^[12-17]. In India people consume dried salted fish, fermented, smoked, pickled meat, use of tobacco, alcohol and *h.pylori* infection is widely prevalent.

In our study male : female ratio was 2.5:1, age distribution is 23 to 87 yrs. Median age affected in this study is 57 years. Most of the patients affected were above 40years(87%). Studies have shown mostly affecting older people. The average age of people when they are diagnosed is 68^[18]. Our study has ten year difference in median age compared other studies, this may be attributed to higher consumption of alcohol and tobacco use. The lifetime risk of developing GC is higher in men (about 1 in 96) than in women (about 1 in 152). Common presentation of GC are abdominal pain and vomiting. Other studies had also reported abdominal pain as most common symptoms^[19-20]. Malignant gastric outlet obstruction(MGOO) was present in 23% of patients. The most frequent cause of MGOO in the Western countries is pancreatic adeno carcinoma (15%–20%), while gastric adenocarcinoma is the most common cause in Asiatic population^[21-22]. Most common sub-site of tumor was body of stomach, but pylorus and antrum combined exceeds body of stomach which is consistent with south indian studies^[23]. Adenocarcinoma was found in all

patients. Moderately differentiated adenocarcinoma(51.1%) was higher as opposed to studies in western world were poorly differentiated carcinoma is common^[24]. Stage wise T3(49.3%) and node was positive in 85% of patients. 99 (44%) patients had distant metastasis, this was concordant with other indian study^[20]. Liver was common site of metastasis followed by omentum and left supraclavicular node, which is consistent with european study^[25]. On multivariate analysis of factors associated with DM are use of tobacco, subsite of tumor and node stage. Regarding treatment 41.3% had curative and 58.7% had palliative treatment. Among radical gastrectomy surgeries, subtotal gastrectomy and distal gastrectomy were more, this data is similar to study from Tata memorial hospital^[26]. D2 lymph node dissection was done in 12.4% of patients. Dutch trial has shown benefit in terms of DFS and OS for D2 lymph node dissection^[27]. Three patients had perioperative chemotherapy based on German FLOT4 and UK MAGIC trail^[28,29]. Twelve patients had preoperative chemotherapy based on French ACCORD07 trail. One third of patients had adjuvant chemotherapy with or without radiotherapy based on SWOG 0116 and CLASSIC trails^[30,31]. Forty one percentage of patients had palliative chemotherapy CDDP with 5 FU +/- leucovorin similar regimen given in French FFDC 9803, Kang YK et al and hsu et al^[32-34]. Limitations of our study are retrospective data and poor follow up due to which the disease free survival and overall survival couldn't be calculated. Further studies are required to analyse the response and outcomes of our patients.

CONCLUSION:

Median age of GC is 57, main risk factors being alcohol intake and tobacco use. Nodal stage, Subsite of tumor location and use of tobacco were found as risk factor for DM. so prevention by avoiding risk factors and early detection by signs, symptoms and endoscopy are necessary. The present study has also highlighted multi modality management involved in treatment. Further studies are needed to analyse outcome and survival.

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