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Origional Research Article

A thirty year study of clinico pathological profile of gastric cancer in Kashmir-A single institute based study

Syed Aabid Hussain[1], Syeed Rayees Ahmad[2], Tariq Ahmed Mala[3]

[1]Post Graduate, Department of General and minimally invasive surgery, SKIMS, Soura, India
[2]Senior resident, Department of general surgery, SKIMS, MCH Bemina.india
[3]Senior resident, Department of General surgery, GMC, Srinagar.India

*Corresponding Author
Syed Aabid Hussain

Abstract: Background: A retrospective and prospective study was conducted; patients were either operated, were advised neo adjuvant treatment or had metastasis and were inoperable. **Method:** Data was analyzed for clinico-demographic information, presenting symptoms & signs. Patients were staged on the basis of Imaging and operative findings. Patients not subjected to surgery were staged with CECT scan & endo-ultrasound. **Results:** Maximum number of patients (3753) belonged to age group of 61-70 years. Only five patients presented with Ca stomach between ages of 21-30 years. Heart burn was the commonest symptom present in 9800 (94%) followed by epigastric pain present in 8860 (85%), loss of appetite present in 7298 (70%), 66% patients presented with weight loss, malena in 3127 (30%) and haematemesis in 1563 (15%), pallor presented with (88%) followed by mass epigastrium (35%).10425 (100%) patients who take dried foods presented with gastric cancer, Smoked food involved 7298 (70%), pickled foods involves 8340 (80%), salted tea involves 9903 (95%), meat consumption involves 10425 (100%). Polypoid growth present in 6255 (60%) followed by ulcerative growth 3961 (38%). Antrum and pylorus were involved 4522 cases, body of stomach involved in 2124, lesser curvature involved in 1562, greater curvature involved in 476 and GE junction involved in 1741 patients. Stage 1A was seen in 180, 1B in 1447, Stage II in 1492, Stage IIIA in 545, Stage IIIB in 406, and Stage IV in 452). The most common operation done was lower partial gastrectomy with billiroth II performed 2909 patients (27.9%) followed by billiroth II subtotal gastrectomy done in 1650 patients (15.83%).Open and close procedure done in 1455 patients (13.96%). Number of Clinically inoperable patients was 1362 (13.06%).**Conclusion**: Incidence of cancer stomach is on rising trend with higher incidence seen in South Kashmir. Intake of mutton and dried foods was seen in all patients. Further studies are needed to know the factors responsible for higher incidence of cancer stomach in South Kashmir region. We recommend mass screening programme in the state by which early gastric cancer can be picked up which can improve the survival**.**

Keywords: Dried food, south Kashmir region, salted tea, stage II.

INTRODUCTION

Carcinoma of the stomach is the fourth most common cancer worldwide after lung, breast and colorectal carcinoma and is the second most common cause of cancer related deaths (Medina-Franco, H. *et al.*, 2000). The incidence varies across different parts of the world due to differences in cultural and food habits. In India it is the fifth most common cancer among males and the seventh most common cancer among females (Rao, D. N., & Ganesh, B. 1998). Kashmir valley is a high prevalence zone of gastric cancer, the incidence of gastric cancer in Kashmir has been reported to exceed all cancers by about 40% & there is three to fourfold increased incidence compared to various metropolitan cancer registries across India (Khuroo, M. S. *et al.*, 1992; Rasool, M. T. *et al.*, 2012; Fuchs, C. S., & Mayer, R. J.1995). The declining incidence of gastric cancer has been observed throughout the world, although patterns vary widely. The incidence is highest in Japan, China, South America and Eastern European lowest in United States (USA 10/ lac year) (John, N. P. 2004; Mercer, D. W., & Robinson, E. K. 2008). The incidence rate for gastric cancer in Islamabad (Southern District is 4.1 to 5.4 times higher in males and 1.2 to 2 times higher in females than those for Kupwara (Northern district (Rao,

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D. N., & Ganesh, B. 1998). Earlier most cases of gastric cancer in the west and USA originated in the distal stomach, recently there has been a steady rise in the incidence of proximal stomach and GE junction, whereas the incidence of distal cancer has remained largely unchanged or has decreased slightly (Mercer, D. W., & Robinson, E. K. 2008). Ninety five percent of gastric cancers were adenocarcinoma; other types were squamous cell carcinomas, lymphomas (non Hodgkin), leimyosarcomas, carcinoid tumors, gastrointestinal stomach tumors (GIST) (Yang, l. 2006). According to Borders (1945) classification gastric carcinoma can be divided into well differentiated, moderately differentiated, poorly and undifferentiated. The relative risk of patients with pernicious anaemia developing gastric cancer is 2.1 – 5.6 (Mercer, D., & Robinson, E.K. 2008). The risk for the development of malignancy in adenomatous polyp is 10 – 20% and increase with increasing size of the polyp (>2cm). Benign polyps associated with atrophic gastritis are also associated with malignancy specifically to intestinal type. Chronic atrophic gastritis and its associated abnormality, intestinal metaplasia, are lesions most closely linked to an increase risk of gastric cancer. Atrophic gastritis usually begins as a multifocal process in the distal stomach, as foci coalesce, a state of reduce gastric acid production results, which may progress to metaplasia, dysplasia and ultimately carcinoma. Patients with prior gastric surgery (Drainage procedures) such as Bilroth II, gastroenterostomy or pyloroplasty, are at approximately four times the average risk (Gangadharan, D. *et al.*, 1967). Other precursor conditions are hypertrophic gastropathy (meneterier's disease) & chronic gastric ulcers.

Diets rich in salted, smoked or poorly preserved foods are associated with increased risk of cancer stomach, whereas diets rich in fruits and vegetables are associated with decreased risk. Foods rich in nitrates, nitrites and secondary amines can combine to N-nitro-compounds which induce gastric tumours in animals. Smokers have 1.5 to 3.0 fold increased risk of cancer stomach. Alcoholics also have an increased risk of developing this disease.

The role of oncogenes and tumour suppresser genes in the pathogenesis of gastric cancer has recently received considerable attention. Allelic deletions of the MCC, APC and P53 tumour suppressor gene have been reported in 33%, 34% and 45% of gastric cancers respectively. Gastric cancer rarely involves mutations in the ras oncogene. Patients with intestinal type cancers have an increased frequency of over expression of epidermal growth factor receptor, erbB-2 and erbB-3. Defuse lesions have been linked to abnormalities of fibroblast growth factor system including the K-sam oncogene (Umeyama, K. *et al.*, 1982).A near universal findings in young patients has been the high frequency of advance lesions and undifferentiated tumours at presentation in comparison with older patients, this has often been attributed to delay in diagnosis (Bedikian, A. Y. *et al.*, 1979). Although shorter period of symptomatology in younger patients is co related with advanced presentations. Gastric cancer in the young patients spreads more rapidly and is more biologically aggressive than in older patients (Matley, P. J. *et al.*, 1988). Prognosis for young patients with gastric cancer is worse than in older patients (Theuer, C. P. *et al.*, 1998).Young patients less likely presents as GE junction growth as compared to antral growth.

METHODS:

This study was conducted in the department of general and minimal invasive surgery, Sheri Kashmir Institute of Medical Sciences Soura, Srinagar, retrospective from July 1987 to May 2015 and prospective from June 2015 to July 2017. Due to lack of a population based cancer registry, data was retrieved from July 1987 to May 2015 from the departmental cancer registry. A total of 10425 patients who had histological documentation of gastric cancer were analyzed. Patients with histology of lymphoma, GIST & melanoma were excluded from the study. All these patients were included with the diagnosis of gastric cancer were either operated or were eligible for neo adjuvant treatment or were inoperable. Data was then analyzed for clinico-demographic information like age, sex, residence, dietary habits, tobacco consumption, association with H. Pylori, alcohol intake, presenting symptoms & signs. Patients were staged on the basis of Imaging and operative findings. Patients not subjected to surgery were staged with CECT scan & endo-ultrasound. TNM AJCC 2010 classification system was used for staging. Morphological variants, histological grades of differentiation (As depicted by the pathologist-Bormann's or Laurens) and location of tumor were other parameters which were analyzed. All the cases were postoperatively managed with IV antibiotics, IV fluids and were discharged after stabilization. Patients were followed and regularly monitored for any complication. Adjuvant treatment was used in most of patients.

RESULTS:

No patients presented with gastric cancer between ages of 0-20 years. Only five patients presented with Ca stomach b/w age of 21-30 years. Maximum no of patients (3753) belonged to age group of 61-70 years [Table 1]. Heart burn was the commonest symptom present in 9800 (94%) followed by epigastric pain in 8860 (85%), loss of appetite present in 7298 (70%), 66% patients presented with weight loss, dysphagia was presented in 1563 (15%), Malena in 3127 (30%) and haematemesis in 1563 (15%), pallor presented with (88%) followed by mass epigastrium (35%) [Table 2].

Among all patients10425 (100%) had history of intake of dried foods, smoked food involved 7298 (70%), pickled foods in 8340 (80%), salted tea in 9903

(95%), meat consumption in10425 (100%), smoking involved in 5942 (57%), and alcoholism in 1772 (17%) [Table 3]. Microscopic appearances of tumor on upper GI endoscopy was polypoid growth present in 6255 (60%) followed by ulcerative growth 3961 (38%). Linitus plastic was present in 209 (2%) patients. Antrum and pylorus were involved in4522 cases, body of stomach in 2124, lesser curvature was involved in 1562, and greater curvature in 476 and GE junction was involved in 1741 patients. Antrum and pylorus were involved in 4522 patients out of whom (Stage 1A was seen in 180, 1B in 1447, Stage II in 1492, Stage IIIA in 545, Stage IIIB in 406, and Stage IV in 452). Among 2124 patients involving body, 658 patients had stage II and 92 patients had stage 1A. Among 1562 patients involving lesser curvature, 493 patients had stage II and 58 had stage 1A. Among 476 patients involving greater curvature, 215 had stage II and 13 patients had stage IIIB. Among 1741 patients involving GE junction 450 patients had stage II and 450 had stage IIIB and 53 had stage IA [Table 3, figure 1]. The most common procedure done was billiroth II lower partial gastrectomy which was performed in 2909 patients (27.9%) followed by billiroth II subtotal gastrectomy in 1650 patients (15.83%).Open and close procedure was done in 1455 patients (13.96%). Number of Clinically inoperable patients was 1362 (13.06%).

Among all patients in our study 63.36 percent were reported from south Kashmir followed by 13.38 % from north Kashmir and 11.2% from Srinagar. As far as the south Kashmir is concerned, 1913 patients were from pulwama, 1753 patients from shopian, 1652 patients were from Anantnag and 1301 patients were from Kulgam. Bandipora was the least affected area with only 369 patients. In 1987 antrum and pylorus was involved in 58.97% cases and GE junction in 9.47% of cases. In 2000 antrum and pylorus was involved in 46. 86% and GE Junction in 19.66% while in 2016 antrum and pylorus was involved in 41.06% cases and GE junction 17.76 % cases of our study [Table 5].

Table 1: Showed age and sex wise distribution

Age Group in Years	No of Cases (10425)	Males (6776)	Females (3649)
0-10			
11-20			
21-30	5	5	
31-40	84	54	30
41-50	1112	533	579
51-60	3440	1548	1892
61-70	3753	3002	751
71-80	1563	1281	282
81-90	468	353	115
91-100			
Total	**10425**	**6776**	**3649**

Table 2: showed clinical features of patients (n=10425)

Symptoms	No of Patients	%age
Heart burn	9800	94
Epigastric pain	8860	85
Loss of appetites	7298	70
Weight loss	6880	66
Dysphagia	1563	15
Malena	3127	30
Haematemesis	1563	15
Pallor	9174	88
Mass epigastrium	3648	35

Table 3: Showed stage of disease with respect to site of tumor.

Stage	Antrum & Pylorus	Body	Lesser curvature	Greater curvature	GE Junction	Total
IA	180	92	58	28	53	411
IB	1447	541	331	81	335	2735
II	1492	658	493	215	450	3308
IIIA	545	191	204	71	179	1190
IIIB	406	318	173	13	450	1360
IV	452	324	303	68	274	1421
Total	4522	2124	1562	476	1741	10425

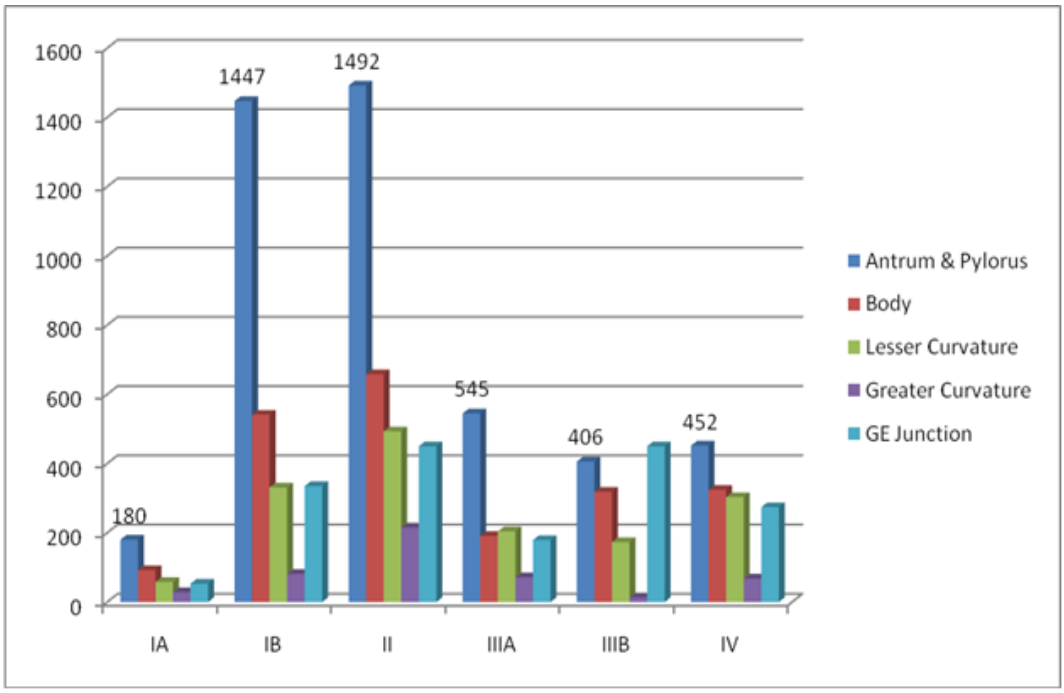

Figure 1: Showed stage of disease with anatomical location

Table 4: showed district wise distribution of patients in Kashmir Valley.

Year	Srinagar	Ganderbal	Bandipora	Baramulla	Kupwara	Budgam	Shopian	Pulwama	Anantnag	Kulgam	Total
1987	26	18	8	10	8	14	28	32	32	20	196
1988	21	10	6	12	9	18	23	33	28	29	189
1989	24	8	8	10	9	19	32	36	26	23	195
1990	21	9	5	13	6	10	35	40	23	26	188
1991	20	8	8	10	7	13	36	35	27	25	189
1992	22	10	4	10	6	15	37	41	25	23	193
1993	18	12	4	8	6	12	40	36	28	25	189
1994	24	10	10	13	7	8	25	36	33	27	193
1995	26	8	15	13	10	8	27	34	26	19	186
1996	26	10	10	14	9	12	18	33	34	25	191
1997	19	7	9	11	6	15	33	37	35	31	203
1998	23	12	8	18	6	12	41	36	36	25	217
1999	24	10	10	15	10	16	39	37	33	36	230
2000	18	16	6	15	10	16	41	47	37	33	239
2001	27	12	4	20	12	18	53	64	38	33	281
2002	29	14	5	21	10	21	61	59	46	29	295
2003	38	16	10	19	12	20	60	74	50	37	336
2004	42	18	10	23	14	24	70	77	56	39	373
2005	41	21	14	24	20	28	70	80	65	45	408
2006	45	20	15	26	22	34	73	80	69	47	431
2007	47	22	18	27	24	32	75	82	73	49	449
2008	49	24	13	29	26	36	78	84	75	52	466
2009	48	23	15	28	25	35	80	88	78	58	478
2010	50	25	19	26	27	33	82	90	82	63	497
2011	52	24	21	27	29	37	86	93	87	65	521
2012	51	26	20	29	26	39	89	95	89	68	532
2013	53	27	23	31	28	38	91	96	91	71	549
2014	52	29	21	32	30	40	93	94	93	75	559
2015	54	30	18	30	29	43	95	97	94	78	568
2016	55	32	20	33	31	42	96	98	96	82	585
2017	28	16	12	17	16	25	46	49	47	43	299
Total	**1073**	**527**	**369**	**614**	**490**	**733**	**1753**	**1913**	**1652**	**1301**	**10425**

Table 5: Showed changing trends in location of cancer stomach.

Cases	Involving Antrum & Pylorus	Involving Body	Involving Lesser Curvature	Involving Greater Curvature	Involving GE Junction	No of Case
1987	97	59	13	7	20	196
88	89	59	12	7	22	189
89	95	63	14	14	23	195
90	96	45	19	4	24	188
91	93	47	17	8	24	189
92	98	44	17	6	28	193
93	101	38	16	5	29	189
94	100	35	20	9	29	193
95	96	24	20	11	35	186
96	94	23	22	14	38	191
97	96	28	23	15	41	203
98	104	29	24	17	43	217
99	108	33	25	19	45	230
2000	112	32	27	21	47	239
1	118	57	35	22	49	281
2	127	55	37	20	56	295
3	146	63	49	20	58	336
4	159	76	52	21	65	373
5	169	79	68	21	71	408
6	176	86	75	20	74	431
7	179	99	83	17	71	449
8	190	101	85	17	73	466
9	196	103	86	17	76	478
10	206	105	88	18	80	497
11	217	108	91	19	86	521
12	221	110	93	20	88	532
13	226	113	96	20	94	549
14	229	115	98	21	96	559
15	231	116	100	22	99	568
16	235	119	103	24	104	585
17	118	60	54	14	53	299
Total	**4522**	**2124**	**1562**	**476**	**1741**	**10425**

DISCUSSION:

Stomach cancer is the most common cancer in the world. In USA it is much less common with 25,000 new cases per year causing 14000 deaths. This means it is about 3% of new cancers in USA each year (Fuchs, C. S., & Mayer, R. J. 1995). The exact reason why one gets stomach cancer is not known. However several risk have been put forward (Khuroo, M. S. *et al.*, 1992; Rasool, M. T. *et al.*, 2012; Fuchs, C. S., & Mayer, R. J. 1995; Mercer, D. W., & Robinson, E. K. 2008). Lack of refrigeration, nitrites and nitrates, intake of pickled and dried foods, helicobacter pylori infection etc are the causative factors. Pain is the most common presentation followed by dyspepsia. Highest incidence has been in the age group of 40-60 years and males are affected three times more than females (Cassell, P., & Robinson, J. O. 1976). Flexible fiber – optic endoscopy is the most accurate method of diagnosis gastric cancer. Further, staging can be done by ultrasonography, CT abdomen and endoscopic ultrasonography (Rao, D.N., & GaneshB, 1998). On CT scan, gastric cancer appears most often as gastric wall thickening. The extension of tumor into spleen, liver, hepatoduodenal ligament, pancreas and diaphragm can be suggested by CT abdomen. Endoscopic ultrasonography is also proving accurate in gastric cancers. The major drawback with endoscopic ultrasonography is the insufficient prediction of lymph node status, with diagnostic accuracy of less than 70%. Overall, 50% tumors involve pylorus and antrum, 20%body of stomach, 20% lesser curvature, 10% cardia and 3% greater curvature. Most of the recent studies show higher rate of involvement of cardia. Adenocarcinoma is the most common histopathologic type of gastric carcinoma, around 95%, which may be further divided into intestinal and diffuse type (ReMine, W. H. *et al.*, 1969). Intestinal type has poor prognosis and occurs more frequently in women and people with blood group A. Resection of the tumor along with adjacent lymph nodes is the treatment of choice in resectable cases (Mishima, Y., & Hirayama, R. 1987). If on exploration, resection of an obstructing lesion is not possible, gastrojejunostomy can still be performed. The study conducted by castello *et al.*, (1977) reported that cancer stomach is seen after the age of 60 years (Costello, C. B. *et al.*, 1977). In our study 45% cases were less than 60 years of age at the time diagnosis with females being effected at younger age group as compared to male. 70% of females in our study were less than 60years of age as compared to 26% males in the same age group. In our study male: female

ratio was 2:1. Allum *et al.*, observed a sex ratio of 3:1(Allum, W. H. *et al.*, 1989). Majority of our patients were farmers. The high risk for cancer with agriculture has been confirmed by Haenzel (1976) and Kiryama (1977) from Japan (Furukawa, H. *et al.*, 1989; Mishima, Y., & Hirayama, R. 1987). The incidence of gastric cancer varies from region to region. 63% of our patients belonged to South Kashmir with highest number of patients coming from Pulwama and Shopian belt. Only 13.38% patients reported from North Kashmir. The exact reason for this is not known. Factors like dietary habits and soil composition are believed to be responsible and need to be studied. 80% of patients were having clinically detected pallor and the high frequency can be due to advanced disease, bleeding and poor dietary habits, and while as only 43% patients were reported anaemic by Castell and Robinson (Cassell, P., & Robinson, J. O. 1976). Pain in the epigastrium was the common symptom in our study as seen in 85% patients. Healy and Bestford (1969) reported incidence of pain in 69.6% patients (Healy, H., & Bostford, M. 1993). Higher incidence of pain in our study could be due to the fact that majority of patients reported late with advance disease and significant infiltration.

In our study all the patients underwent diagnostic esophago-gastro duodenoscopy (EGD). Polypoid growth was seen in 60.18% patients, ulcerative growth in 37.75% patients with linitus plastica in 2.3% patients. This is in contrast to study conductedby Paul Casell *et al.*, (1976). In their study ulcerative lesion was seen in 51%, infiltrative lesion in 32% and polypoid lesion in 17%. 45 patients of early gastric cancer were picked on endoscopy. The early gastric cancer is defined as cancer limited to mucosa and submucosa irrespective of lymph node status. Japanese have reported 30-40% incidence of early gastric cancer.While as non-Japanese have reported 5.10% incidence of early gastric cancer. This high incidence of early gastric cancer is Japanese literature is because of mass screening of population for carcinoma stomach which was introduced in mid 1960. In our study very low incidence of early gastric cancer is due to the fact that we are not having any screening programme majority of our patients report late and there is no availability of endoscopic facilities at primary care levels. Majority of our patients were having pyloric growths (49%) followed by body (21%). This is in agreement to that of Gangadharan Dowson, and Longmire, while Casell and Robinson (1976) have reported that body was more commonly involved (Gangandharan, D, *et al.*, 1967; Longmire. *et al.*, 1986; Cassell, P., & Robinson, J. O. 1976). 96% of our patients were having adenocarcinoma with remaining 4 % having signet ring cell carcinoma. In our study 59% patients were resectable and various types of gastrectomies were done. Out of 59%, curative resection was possible in only 6-7% patients while as palliative resections were done in 42 to 43% patients. In 14.29% patients only bypass procedure was done in the form of anterior-gastro-jejunostomy, while as in remaining 27% no procedure was done, as they were found unresectable. Brooks *et al.*, and Inberg *et al.*, reported a respectability rate of 42.5% and 45.1% respectively (Brooks, S. *et al.*, 1965). On the other hand Yamado *et al.*, found 80% patients resectable at laparotomy (Maruyama, K. *et al.*, 1987).

CONCLUSION

The number of cases admitted with diagnosis of cancer stomach during 1987 was only 196. There after there was as steady rise in the number of cases every years and the number of cases admitted with cancer was 585 during the year 2016. As far as the geographical distribution is concerned, the disease was found to be more in certain areas of the valley, particularly the South Kashmir, while as lesser number of cases reported to us from the North Kashmir. Intake of mutton and dried foods was seen in 100% patients, while as alcoholism was seen in only 17% patients. Pain was the most common presentation and was seen in 85% patients followed by loss of appetite in 70% and pallor in 89% patients. In view of involvement of proximal stomach with upward trend we recommend mass screening and further studies to know the factors responsible for higher incidence of cancer stomach in Kashmir valley particularly South Kashmir by which early gastric cancer can be picked up which can improve the survival.

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