CLINICO- DEMOGRAPHIC PROFILE OF GASTRIC CANCER IN KASHMIR

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ABSTRACT: BACKGROUND: Gastric cancer (GC) is the fourth most common cancer in the world. Worldwide it constitutes the second leading cause of cancer related death in both the sexes. There is a wide demographic variation seen with GC, with Asian countries like China alone representing almost 42% of the world's GC burden. Over the years the western nations have reported a decrease in the incidence of GC but with an increasing incidence of proximally located GCs, whereas most of Asian countries have distally located cancers. AIMS & OBJECTIVES: To Analyze the 'Clinic-Demographic' profile of gastric cancer in Kashmir valley **MATERIALS & METHOD**: We conducted an analytical, non-randomized, cross-sectional study on the Clinico-Demographic profile of 330 patients with primary GC who reported to our OPD between July2011 to July 2015. **RESULTS:** Over a period of four years 330 patients of primary GC were analyzed. Majority were males. Mean age of the patients was 62 years. Majority were smokers & non-vegetarian and none consumed alcohol. Tumor location was proximal in 13% & distal in 62% with no gender predilection. Median age of the patients was 60 years. Commonest presenting symptom in both the sexes was pain abdomen. Demographic shifts reported in western literature were not consistent with our data. **CONCLUSION:** Most of our patients present in late stage with adverse clinicopathological factors. The median age group of enrolled patients is lower than those in the west. Most of the patients are males, from a rural background with more than one symptom, out of which pain abdomen, weight loss are commonest. The trend of proximal shift in the site of cancer as projected by other studies was not observed in our population. **KEYWORDS:** Gastric cancer, Demography, Incidence, Kashmir valley.

INTRODUCTION: The incidence of GC varies in different parts of the world & among various ethnic groups. It is the third most common cancer after breast & lung cancer & second most common cause of cancer related death after lung cancer in Asian nations.⁽¹⁾

In India it is the fifth most common cancer among males & seventh most common cancer among females,⁽²⁾ Incidence of GC varies widely among various regions in India, a finding which authors attribute to its multiethnic culture & diverse food related habits. The southern & northeastern states of India have reported highest incidence of GC comparable to the high incidence areas of the world.⁽²⁾ Kashmir valley is a high prevalence zone of GC,^(3,4) the incidence of GC 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.^(3,4)

The aetiology of GC is multifactorial and various dietary and environmental factors are implicated in the development of GC.⁽⁵⁾ Poor food preservation has been seen to be associated with increased incidence of GC, as has been smoked meat & dried fish consumption- a habit quite prevalent in Japan.⁽⁶⁾ Over the years the role of H. Pylori is being increasingly recognised as a causative agent in GC,⁽⁷⁾ however, the prevalence of this infection varies worldwide being as low as 10 per cent in developed western nations to higher than 80 per cent among the indigent populations of many developing countries.⁽⁸⁾ Profile of gastric cancer has changed over the years with respect to site,

gender & mortality, with western literature suggesting an increased incidence of proximally located cancer, poorly differentiated histology & increased mortality in females.⁽⁹⁾ Our study was undertaken to analyse the demographic trends of GC over the years & corroborate the results with the data outside Kashmir & western literature.

MATERIAL AND METHODS: This study was conducted in the department of Radiation Oncology, Government Medical College Srinagar, from July 2011 to July 2015. Due to lack of a population based cancer registry data was retrieved from the departmental cancer registry. A total of 330 patients who had histological documentation of GC were analysed. Patients with histologies of lymphoma, GIST & melanoma were excluded from the study. Included in this study were patients who were either operated, were eligible for neo adjuvant treatment or inoperable & metastatic at presentation. Data was then analysed 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 surgical pathology report & imaging. 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-Bormanns or Laurens) and location of tumor were other parameters which were analysed.

RESULTS: This study included 330 patients who had histologically proven gastric malignancy. Of 330 patients analysed 251(76%) had been subjected to surgery whereas 79(24%) were either stage IV at presentation or inoperable. Patients with histologies of lymphoms, GIST & melanoma were not included in the study. Male to female ratio was 2.4: 1. The age distribution varied from 28 to 96 years with the youngest patient being a female one. The age and sex distribution is shown in table 1, 2. Majority of the male patients were in the age group of 40-60 years (50%), followed by >60 years age group (40%) & <40 years constituted 10% of male patients whereas majority of the females were in the age group of >60 years. Out of 330 patients 3% had a family history of GC or any other cancer in the family.

Dietary intake of meat was seen in 95%(315) of patients whereas 81%(271) had history of tobacco consumption in one form or the other. Eighty percent (270) patients had a rural background & had history of consumption of dried vegetables (Brassica Olerecea)-an age old tradition of preparation. Cigarette smoking was equally distributed amongst rural & urban population whereas 'Hooka', smoking was predominant in rural population. Of the fifteen nonsmokers three were females. Only 22 patients had been evaluated for H. Pylori of which only seven were positive. The socio- demographic profile of patients is shown in table 3.

Pain abdomen was the commonest presenting symptom in over two thirds (67%) of the patients; followed by early satiety (54%), weight loss (35%), vomiting (30%), dysphagia (25%), anorexia (25%), melena (20%).

Patients with distally located tumors had vomiting as a prominent symptom whereas patients who had tumors located proximally had dysphagia as prominent symptom. Generalised weakness was complained by 80% of the patients and over two thirds of patients had more than one presenting symptom.

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Pallor was noted in nearly 60% of the patients at presentation & 20% of the patients had a palpable abdominal lump at presentation. Palpable peripheral lymph-adenopathy was seen in 5% of the patients.

Pyloric antrum was the commonest site of GC in our study with 62% patients having growth in antrum, followed by body (25%), fundus & cardia 8% & 5% respectively. Antrum was the commonest site in both males (64%) & females (36%) with 130 & 74 patients respectively.

Commonest histology was adenocarcinoma in 95% of the patients with 5% having its variants like adeno-squamous, squamous & adenocarcinoma with neuro-endocrine features.

'Ulcerated' appearance was the commonest of all the morphological variants (35%), 'infiltrative' (28%), 'polypoid' (25%) & 'fungating' (12%).

Commonest histological variants were moderately differentiated (54%), poorly differentiated (32%) & well differentiated (14%).

Of the forty four (13%) patients who had proximally located tumors (Cardia & fundus) poorly differentiated histology was seen in 34(10%) patients.

Majority of the patients (55%) had T3 disease at presentation, followed by T2 (25%), T4 (18%), T1 (2%). N2 was the predominant nodal stage with 50% followed by N3 (24%), N1 (20%) & N0 (6%). Over 24% of the patients presented with stage IV disease. Liver was the commonest site of metastasis (48/80) followed by Virchows node positive (25/80), peritoneal metastasis (22/80) & multiple metastasis (More than one site of metastasis). Of the eighty patients who presented with stage IV disease, 54 had poorly differentiated histology.

DISCUSSION: Of the ten lakh patients who are diagnosed annually with GC nearly seventy percent succumb to the disease.⁽¹⁰⁾ It accounts for nearly ten percent of all cancer related deaths worldwide.⁽¹⁰⁾ The incidence of GC in India is low as compared to that of western nation with close to 35000 new cases being diagnosed annually. It is estimated that by the year 2020 approx. 50000 new GC cases will be reported in India annually.⁽¹¹⁾ The southern Indian states have reported high incidences of GC but of late the north eastern states have been reporting high incidences of GC.⁽¹²⁾

Kashmir valley has a high prevalence of GC & as per hospital based data in Kashmir collected over a period of fifteen years, GC constituted nearly fifteen percent of all malignancies in males & about 12 percent in females. It was reported to be the second most cancer among males & third most common cancer among females.⁽¹³⁾ Overall it was the third most common cancer reported in Kashmir. ⁽⁴⁾ However a changing trend was noted with respect to the site of the malignancy with proximal cancers (GE Junction & cardia) constituting a frequent site of disease.⁽¹³⁾ corroborating the same data from western nations,⁽¹⁴⁾ however, in our study pyloric antrum was the commonest site (60%) in both the sexes & no significant increase in the incidence of proximal cancers (13%) was noted, though GE Junction cancers were not included in the study. Age & sex parameters have remained same over the last twenty years in Kashmir,⁽¹⁵⁾ with most of the patients falling in fifth & seventh decade of life with majority being males. In our analysis majority of the male patients were in the age group of forty to sixty years & males constituted over sixty percent of the patients.

Earlier peculiar food habits like overwhelming use of pickled vegetables, spice cakes (Wur), smoked meat, poorly preserved food & consumption of dried vegetables were implicated as the possible causative agents. Over the years the methods of food preservation has improved in Kashmir valley but it hasn't translated into a statistically significant decrease in cancer incidence, a finding which partly may be attributed to non-dietary factors or the unique geography of the valley.⁽¹⁶⁾

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H. Pylori infection is considered a strong risk factor for GC.⁽¹⁷⁾ Approximately 50 percent of the world's population has been estimated to be infected with H. Pylori.⁽¹⁸⁾ The prevalence of H. Pylori infection in India is seen to be around fifty to eighty percent, but the incidence of GC is comparatively low indicating mixed results for the association between H. pylori and GC.⁽¹⁹⁾ Epidemiological studies have shown mixed results for a definite association between H. Pylori and GC in approximately 50% patients, and a negative relationship in the remaining patients.⁽²⁰⁾ A study in North India on the prevalence of H. Pylori in patients with gastric carcinoma was assessed and correlated with gross appearance and histological types. It revealed that the prevalence of H. Pylori in controls was slightly higher than that in the patient group (80% Vs. 78%). It was inferred that the prevalence of H. Pylori association was greater in diffuse type GC than in intestinal type (86% Vs. 68%).⁽²¹⁾ Pertinently countries like India & Bangladesh being a high prevalent area for H. Pylori don't have proportionate incidence of GC unlike Japan where cause- effect relation could be observed, implying other factors playing a concomitant role along with H. Pylori infection in GC.⁽²²⁾

Prevalence of H. Pylori in a cohort of fifty patients with APD in Kashmir valley revealed 76% prevalence in DU, 50% in GU & 100% in multiple ulcers,⁽²³⁾ In another study in Kashmir, H. Pylori was tested in 33 patients of which only 13 were positive, underscoring any significant association between H. Pylori & GC.⁽²⁴⁾ In our study we observed that of 330 patients 80 patients had preexisting acid peptic disease (APD) symptoms of which only 22 had undergone H. Pylori screening (Majority were not screened for H. Pylori) & only 7 were H. Pylori positive. This excludes all those patients who didn't have APD symptoms. So any association of H. Pylori with GC & its demographic variables thereof could not be inferred in the present context.

Laurens histomorphic classification divides GC into diffuse (Undifferentiated) or the intestinal type. Worldwide the two types are seen to have a distinct clinical behaviour & treatment outcome.⁽²⁵⁾ The diffuse type occurs in all age groups with equal gender distribution, unlike the intestinal type, which predominates in males and older persons. In our study intestinal adenocarcinoma was the predominant histology in the antrum whereas diffuse type involved the corpus or proximal stomach. Of the eighty patients who presented with a stage IV disease, fifty four had a poorly differentiated or diffuse histology, thus suggesting an aggressive clinical behaviour of the diffuse morphology. As per a European literature increase in poorly differentiated histology was seen in proximal cancers & increase in well differentiated tumors in distal antral cancers over a period of ten years.⁽²⁶⁾ In the analysis conducted by Romana et al overall percentage of poorly differentiated adenocarcinomas was on an average 27% & the increasing trend of lesions at cardia was not observed as against the western literature.⁽¹⁵⁾ The percentage of poorly differentiated tumors in our study was 32% implying an increase in poorly differentiated histology over time.

The exact demography of GC with regards to its incidence cannot be projected with a certainty with the available data in this study because of lack of a population based cancer registry & a separate hospital based cancer registry available in the valley. Patients at times are registered at both the centres which create erroneous data of double registration. However with the sample size available, dietary association, association with smoking, subsite shift of the tumor, gender predilection, trends of dominant histological variant, correlation of aggressive histologies with stage at presentation are the parameters which could be inferred.

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This study however needs further recruitment of patients so that the sample size can be large enough to derive an impression regarding clinico-demographic profile of GC in valley & denominators affecting it.

CONCLUSION: This study points out the fact that most of our patients present in late stage with adverse clinicopathological factors. The median age group of enrolled patients is lower than those in the west. Most of the patients are males & from a rural background with more than one symptom, out of which pain abdomen, weight loss are commonest. The trend of proximal shift in the site of cancer as projected by other studies were not statistically significant in our study; however of the forty four proximally located cancers, thirty four had poorly differentiated histology & same (Diffuse) histology was found in over two thirds of the stage IV patients. No conclusion could be drawn as regards to the association of H. Pylori with GC, as number patients who were screened were very less.

SEX	Number(Percentage)
Male	233(70)
Female	97(30)
Table 1: Showing Sex Distribution	

Age in years(Males)	Number(Percentage)	
40-60	117 (50)	
>60	93 (40)	
<40	23(10)	
Age in years(females)		
40-60	12(13)	
>60	74 (76)	
<40	11 (11)	
Table 2: Showing Age and Sex Distribution		

Residence	
Rural	270 (81%)
Urban	60(19%)
Non-Veg	315(95%)
Tobacco	
Total	315(95%)
Rural	263(83%)
Urban	52(17%)
Cigarette	
Rural	61 (Includes 20 'hooka' smokers) (23%)
Urban	31(60%)
'Hooka'	
Rural	202 (Includes 20 cigarette smokers) (76%)
Urban	21(40%)
Table 3: Showing Socio- Demographic Profile of Gastric Cancer Patients	

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