

RESEARCH COMMUNICATION

Gastric Cancer in Kashmir

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Abstract

Gastric cancer has been reported to be a highly prevalent malignancy in Kashmir, where together with esophageal cancer it accounts for more than 60% of all cancers, much higher than in other parts of the region. Particular life style habits like consumption of salted tea and tobacco smoking by hukkah, as well as *Helicobacter pylori* infection, are often mentioned in the context of risk factors. However, the majority of the population does not consume alcohol and the prevalence of *H. pylori* does not appear to explain the high incidence of gastric cancer in the population. Other prevalent habits of gastric cancer patients are presented here along with demographic and tumor details. In future, well designed studies of incidence rates (population based) are essential along with investigations of reported and suspected risk factors.

Keywords: Gastric cancer - Kashmir - lifestyle factors - tobacco

Asian Pacific J Cancer Prev, 12, 303-307

Introduction

Gastric cancer is the fourth common cancer and the second most common cause of cancer deaths worldwide (Peter Boyle and Bernard Levin, 2008). The geographic distribution of gastric cancer is characterized by wide international variations. High-risk areas include Japan, Korea, and China, as well as Central and South America. Gastric cancer incidence is decreasing in many countries, however the overall five year survival rates remain low, even in the United States the five year survival rate is only 24%. Incidence rates are low in southern Asia, North America, and Africa (Parkin et al., 2005). Globally, the highest rate in males was seen in Japan-80/100,000 and the lowest rate was in Thailand, around 3/100,000 population. Among females also the highest rate of 31/100,000 was in Japan and the lowest of 1.0 was in Trivandrum, India (Curado et al., 2007).

The variations in gastric cancer incidence seen in India have been quite marked (National Cancer Registry Programme, 2010). In Table 1, the Age Adjusted Incidence Rate of gastric cancer from Indian registries are shown.

The registry at Dindigul is managed by Cancer Institute, Chennai (Swaminathan et al., 2005). All others are in the National network of registries under the Indian Council of Medical Research.

As reported by the population-based cancer registries in India 2006-2008, stomach cancer is one among the 5 leading cancers in males in Bangalore, Chennai, Dibrugarh, Kamrup Urban, Kollam, Dindigul, Aizawl, Mizoram, Sikkim and among females it is the third most

common cancer in Barshi, Chennai, Mizoram and Sikkim. The highest age adjusted incidence rate seen among males

Table 1. The Age Adjusted Incidence Rate of Gastric Cancer - Indian Data

Incidence of Gastric Cancers - Indian Data 2006-2008			
Place	Male	Female	M:F
Ahmedabad (R)	1.0	0.6	1.7:1
Aurangabad	1.6	1.2	1.3:1
Barshi Expanded	1.6	1.0	1.6:1
Ahmedabad (U)	1.7	0.9	1.9:1
Barshi	2.1	2.3	0.9:1
Bhopal	2.8	1.5	1.9:1
Nagpur	2.9	1.7	1.7:1
Kolkata	3.1	1.8	1.7:1
Delhi	3.2	1.4	2.3:1
Pune	3.8	1.4	2.7:1
Mumbai	4.3	2.7	1.6:1
Thiruvananthapuram	5.0	1.2	4.2:1
Kollam	6.3	1.4	4.5:1
Cachar District	6.4	1.2	5.3:1
Dindigul	7.0	2.5	2.8:1
MR Excl. Imphal West	7.5	4.4	1.7:1
Manipur State (MR)	7.8	4.6	1.7:1
Imphal West	8.6	5.3	1.6:1
Dibrugarh	9.4	5.1	1.8:1
Bangalore	9.5	5.6	1.7:1
Kamrup Urban District	10.6	4.3	2.5:1
Chennai	11.8	6.0	2.0:1
Sikkim	12.3	11.0	1.1:1
Mizoram Excluding Aizawl	36.2	18.2	2.0:1
Mizoram State	42.9	20.5	2.1:1
Aizawl	55.4	24.4	2.3:1

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in this report was 55.4/100,000 and in females it was 24.4/100,000. Between lowest and highest rates there was more than 30 to 40 times difference.

In the National Cancer Registry Programme, the incidence rate and distribution of stomach cancer in Kashmir are not available due to lack of both population and hospital based cancer registries.

However, two studies from Kashmir could be quoted in this regard (Azra and Jan, 1990; Khuroo et al., 1992). In 1990, analyzing the histologically proved cancer cases seen during 1983-1987 in the Pathology Department of Sher I Kashmir Institute of Medical Sciences, Srinagar, it was reported that stomach cancer formed 31% of all cancer in men and 18% in women; (M - 687, F - 192) M:F is 3.6:1 (Azra and Jan, 1990). However the adjoining Jammu region in South had recorded only 1.6% of all cancer in men and 1.3% in women as stomach cancer (Kapoor et al., 1993). The only population based study from Kashmir analyzing data obtained during 1986-89 observed that the age adjusted stomach cancer incidence among males was 36.7 and among females it was 9.9/100,000 (Khuroo et al., 1992), indicating that there is a high rate of gastric cancer in Kashmiri population compared to other parts of the country. Even within the state the various districts showed varying rates. Different dietary practices and peculiar life style habits of the natives has been implicated for such variation. Such remarkable differences called for special studies

Globally, the well known epidemiologic observations in gastric cancer include (a) when migrants from a high risk country move to a low risk country (Japan to America) the incidence rate makes remarkable reduction and reaches almost equal to the rates in the low risk countries (Haenszel et al., 1972). (b) Those with blood group A are at high risk (Edgren et al., 2010) (c) Adenocarcinomas are the most frequent morphologic type with two distinct subtypes viz. diffuse and intestinal type. Of these the intestinal type is considered as the epidemiologic type influencing the changes in incidence (Lauren, 1965). (d) Salted pickles, heavily spiced foods and intake of tea have also been incriminated (Khuroo et al., 1992; Peter Boyle and Bernard Levin, 2008). (e) Tobacco smoking has been identified as a risk factor for Stomach cancer (IARC, 2004). (f) Use of vegetables and fruits are factors which are believed to reduce the risk (Terry et al., 1998; Peter Boyle and Bernard Levin, 2008). (g) The role of *Helicobacter Pylori* which is a most suspected factor now has attracted the attention of oncologists and it is considered as a significant causative factor. A relative risk of 5.9 for *H pylori* presence has been reported for stomach cancer (*Helicobacter* and cancer collaborative group, 2001).

The present preliminary observations are on the distribution of some of the environmental factors suspected in the genesis of stomach cancer as seen in Kashmiri population.

Materials and Methods

A descriptive study of stomach cancer was conducted over a period of one year - March 2006 to Feb 2007

jointly by the Department of Community Medicine and Gastroenterology Division of General Medicine of Government Medical College, Srinagar. Eighty one patients with histologically diagnosed stomach cancer were interviewed using a pre-tested semi-structured questionnaire and relevant demographic, dietary and environmental data were recorded. Information regarding symptoms, family history of stomach cancer among first degree relatives, food consumption pattern, smoking habits, consumption of peculiar foods like sun dried vegetables, smoked fish, sun dried fish, powdered roasted corn and rice, wild vegetables, intake of salted alkaline tea, food preservation methods and intake of fruits were recorded. *H. Pylori* factor was tested among 33 patients. The data was tabulated and analysed using relevant tests in statistical software SPSS 11.0 version.

Upper gastrointestinal endoscopy was performed in all patients, using fiberoptic endoscope (Olympus GIF V2). Esophago-gastro-duodenoscopy was performed using 2% xylocaine jelly for local anesthesia. After receiving a written consent, the endoscopy was performed, the endoscopy was performed by an experienced Gastroenterologist. Each patient was made to lie down comfortably on the bed in left lateral position with face towards the endoscopist. The endoscope was passed into esophagus through mouth gag supported into the patient's teeth. The endoscope was then guided into the stomach. Once the growth was seen, multiple biopsies (at least eight) were taken from the growth for histopathology. Multiple biopsies were also taken from normal looking mucosa adjacent to the growth for determining the *Helicobacter pylori* status. Biopsy material was fixed in 10% formalin at room temperature and later on processed for histopathology.

For *Helicobacter pylori* testing, the rapid urease test was used, by using *Helicobacter pylori* kit TM manufactured by Allied Marketing Corporation Kolkata, with sensitivity of 90% and specificity of 90%. A presence of infection was ascertained by color change from yellow to red within a time period of 15 to 20 minutes.

Results

During the study period there were 81 patients (males - 62, female - 19) with a male to female ratio of 3.3:1. In Table 2 the age distribution of the patients is given. The average age of male patients was 61 years but in females it was 63 years slightly higher than that of males.

The socio-demographic profiles of patients are shown in Table 3. Kuppuswami's social class scale is based on education of head of family, per capita monthly income and occupation. Nearly three-fourths of the patients were illiterate. Almost 77% of patients were from poor and middle class. Among the occupational groups, 26 had exposure to insecticide.

In this valley, the tobacco addiction is very frequent as it is a very popular habit. Hukkah smoking is the popular form of tobacco smoking and is used by males and females alike. Tobacco smoke is passed through water before it is inhaled through a tube. In Table 4, tobacco habit pattern of patients are given.

Table 2. Age Distribution of Gastric Cancer Cases

Age	M	F
20-24	1	0
25-29	2	0
30-34	0	0
35-39	0	0
40-44	0	1
45-49	3	3
50-54	12	0
55-59	2	1
60-64	17	4
65-69	9	3
70-74	13	6
75+	3	1
Total	62	19
Average Age	61	63

Table 3. Socio-demographic Profile of Stomach Cancer Patients

		No.	%age		
Sex	Male	62	76.5		
	Female	19	23.5		
Residence	Urban	23	28.4		
	Rural	58	71.6		
Education	Illiterate	59	72.8		
	Primary	4	4.9		
	Middle	9	11.1		
	Higher Secondary	8	9.8		
Occupation	Graduate	1	1.2		
	M	F	T		
	House-wife	0	17	17	21.0
	Government employee	8	1	9	11.1
	Farmer & Agricultural laborer	31	1	32	39.5
*Socioeconomic class	Others	23	0	23	28.4
	Upper High	1	1.2		
	High	19	23.5		
	Upper Middle	27	35.3		
	Lower Middle	29	35.8		
Poor	5	6.2			

* Kuppuswami's social class (2007)

Table 4. Pattern of Tobacco Use among Gastric Cancer Patients

Habit	M	F	Total
Hukkah	25	7	32
Cigarette	10	0	10
Snuff	4	3	7
Mixed	16	0	16
Absent	7	9	16
Total	62	19	81

Among male patients, almost 90% (55/62) used tobacco in some form and among females 53% (10/19) used tobacco. Female tobacco users were mainly hukkah smokers (7/19) and three had the habit of nasal use of snuff (powdered tobacco). Among the 81 patients, only 16 (20%) did not give any history of tobacco use. Family history of cancer was reported in 7.4% of cases.

The dietary pattern of cases is shown in Table 5. Among the 81 patients only one reported as a strict vegetarian. Among the food items consumed more popular ones were: smoked fish (35.8%), dry fish (48.1%), pickles

Table 5. Dietary Pattern of Stomach Cancer Patients

Special dietary habits	No.	%	
Sun dried vegetables	71	87.3	
Sun dried fish	39	48.1	
Pickles	54	66.7	
Smoked fish	29	35.8	
Powdered corn	37	45.7	
Wild vegetables *	13	16.0	
Salt tea	<4cups/day	26	32.1
	>4cups/day	55	67.9
Fruits	>3/week	22	27.2
	<3/week	59	72.8

**Lisa-Amaranthus caudatus*; *Nunar- Portulaca oleracea*; *Sochal-Malwa sylvestris*; *Hand- Taraxacum officinale*; *Abuj-Rumex nepalensis*; *Gule- Plantago lanceolata*; *Cruss- Centurea iberica*

Table 6. Clinical Presentation of Gastric Cancer Cases

		No. of Patients (n=81)	% (n=81)
Symptoms	Dyspepsia	62	76.5
	Anemia	66	81.5
	GI Bleed	34	41.9
	Weight Loss	28	34.5
	Vomiting	29	35.8
Site of Lesion	Loss of appetite	34	42.0
	Proximal Stomach	34	42.0
	Distal Stomach	37	45.7
	Mid Stomach	5	6.2
Type of Lesion	Diffuse	5	6.2
	Ulceroproliferative	29	35.8
	Proliferative	21	25.9
	Ulcerative	25	30.9
Infiltrative	6	7.4	

(66.7%) and roasted powdered corn and rice (45.7%). There is also a group consuming wild vegetables (Table 5). Distribution of patients as per consumption of wild vegetables show that only 13 (16%) of patients were consuming wild vegetables.

Salted tea drinking is a special habit among the population. The salted alkaline tea is prepared from green tea in water boiled for hours along with a small amount of sodium bicarbonate and then brewed until a reddish brown coloured extract is obtained. This extract is stored for a long period and used over many days by mixing with water, salt and little milk and taken while it is still hot. It is not unusual for people taking even up to 10 cups a day. This local favorite drink is prepared in a nickel plated copper vessel (samovar) or in aluminium vessel. In the present study, more than 2/3rd of the patients had the habit of consuming >4cups/day.

Consumption of fresh fruits by stomach cancer patients was found to be relatively low with only 12 patients (14.8%) consuming fruits >4 times/week. Compared to this, 52 (64.2%) patients were consuming less than two times a week. Almost 77% had regular food intake. 79% used copper vessels for cooking.

In Table 6, the clinical presentation, site and type of lesion of stomach cancer patients are shown. Weight loss is a very common sign for stomach cancers. In the current series, 28 patients (35%) reported weight loss. At the time of diagnosis patients presented with multiple symptoms like dyspepsia (76.5%), loss of appetite and vomiting

Table 7. Histopathology of Gastric Cancers

HPE (Adenocarcinoma)	M	F	Total
Well Differentiated	31	9	40
Moderately Differentiated	7	2	9
Poorly Differentiated	24	7	31
Mixed	0	1	1
Total	62	19	81

Table 8. H. Pylori Test Results - 33 Patients

	H. Pylori test	
	Positive	Negative
Part of Stomach		
Distal Stomach	6	8
Others	7	12
Age (in years)		
Mean Age	62.6	59.8
Tobacco Habit		
Hukkah	8	9
Snuff	2	3
Cigarette	0	2
Hukkah+Cigarette	0	0
No habit	3	6
Total	13	20

(35.8% each). On physical examination, anaemia was the most common sign and was present in 66 (81.5%), ascites was present in 9 patients (11.1%), epigastric mass in 8 (9.9%) and one patient had splenomegaly.

Regarding distribution of cancer within the stomach, Distal stomach was involved in 45.7%, Proximal stomach in 42% of patients, Middle stomach and Whole stomach were involved in 6.2% each. Among the common symptom, ulceroproliferative type was seen in 36%, ulcerative lesions were 31%.

In Table 7 the microscopic verification diagnosis is given. Histopathologically nearly half of lesions were well differentiated adenocarcinoma.

H. Pylori was tested in 33 patients. Among them 20 were negative and 13 were positive. The results are shown in Table 8. The average age of positive patients was 62.6 years and of negative patients was 59.8yrs, 3 of 13 positive patients were women, 6 had distal stomach involvement. In the *H. Pylori* negative group there were 20 patients of whom 15 were males and 5 were females.

Discussion

Globally, variations observed in gastric cancer incidence in populations have provided leads to study the factors associated with stomach cancer.

Kashmir, one of the three provinces of Jammu & Kashmir state is in the northern most part of the country and the beautiful hilly terrain, gifted natural settings and the peculiar life style of the people are significant. Almost 95% are Muslims, 4% Hindus and the rest follow Sikh religion. Alcohol is not consumed by Muslims.

Earlier reported studies indicated a high prevalence of stomach and esophageal cancer. The only reported incidence data also highlighted the incidence of stomach cancer, with a high male to female ratio, 3.5:1. In the present series the male to female ratio was 3.3:1 almost similar to what was reported earlier. Another often

reported causative factor is tobacco use. Studies reported from south India (Gajalakshmi and Shanta, 1996) as well as from North East states (Phukan et al., 2005) indicate cigarette smoking as a significant risk factor. In a Meta analysis (Trédaniel et al., 1977) have shown that there was a 1.5 times risk for smokers to develop stomach cancer. In the present study a large percentage of tobacco smokers used Hukkah. Dietary components like hot spicy foods, salted pickles which are used by a large population have been identified as high risk factors as these expose the person to dietary amines and nitrates (Trichopoulos et al., 1985; Hu et al., 1988). The predominant (90%) histology type is adenocarcinoma.

There have been several studies on *H. pylori* status in the Kashmiri population. A study evaluated 50 patients for *H. Pylori* infection reported *H. pylori* positivity among 17 (34%) as compared to 30 controls where *H. pylori* was present among 33%, underscored that there may not be a significant association between *H. pylori* status in this group (Malik et al., 1997). In the present study also there was no significant difference in *H. pylori* prevalence between the tested groups. Among the 33 *H. pylori* tested patients 39% only were positive and 61% was negative which was again similar to the previous observation. In a review of *H. pylori* studies in relation to gastric cancers Miwa et al., 2002 observed that the established link between *H. pylori* and stomach cancer in Japan is not repeated in countries like India and Bangladesh which had a high prevalence of *H. pylori* but low gastric cancer. Such phenomenon is identified as an Asian Enigma and Holcombe 1992 termed such a situation as African Enigma also. It has been suggested that (Prinz et al., 2006) infection with certain strain types in the presence of genetic polymorphisms leading to a heightened inflammatory response is associated with a dramatically increased relative risk to document gastric cancers. It may be mentioned that in the absence of *H. pylori* associated carcinogenic stimulus the dietary and tobacco habit pattern may come into prominence especially because a large percentage of the cases were tobacco users.

Various studies have also identified tobacco use and certain food preparations especially salted pickled vegetables as risk factors. In a case control study from Chennai south India, alcohol and pickled food consumption were shown to be significant risk factors. (Sumathy et al., 2009) and cigarette smoking was not observed to be a risk factor. However, in another case control study from Chennai in 1996, smoking emerged as an independent risk factor (Gajalakshmi and Shanta, 1996). In the Kashmiri population the use of pickles forms an important constituent of daily food.

Another important cancer identified in Kashmir population is esophageal cancer - age adjusted incidence rates for male were 43.6/ 100,000 and female 27.9/100,000. Both these are higher than all the rates reported by the National Cancer Registry Programme. The high incidence rates seen for both esophagus and stomach cancers points to the possibility of presence of common high risk factors like diet and tobacco use. The low relative frequency of stomach cancer noted in the adjoining Jammu region has to be noted in this regard.

The role of genetic factors in the etiology of GI cancers is highly suspected. In the present study 7.4% of the cases had a family history of stomach cancer. The Kashmiri population may have a genetic profile similar to the population in the neighbouring northern mountainous region.

In conclusion, the present preliminary observations highlight the need for analytical studies and *H. pylori* status among this high risk population along with their dietary and tobacco consumption patterns. A positive association of gastric cancer occurrence with *H. pylori* status in Kashmir is not visible from this study as well as from that of an earlier study. Further studies are warranted with regard to the suspected high risk factors and their interaction.

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