

# High incidence of oesophageal and gastric cancer in Kashmir in a population with special personal and dietary habits

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## Abstract

Over a three year period (1 July 1986 to 30 June 1989) all newly diagnosed and histologically proved cases of oesophageal and gastric cancer were recorded prospectively. Some 1515 cases of oesophageal cancer (1050 men and 465 women) and 966 cases of gastric cancer (789 men and 177 women) were registered. Seven patients had simultaneous oesophageal and gastric cancer. Age standardised incidence rates for oesophageal cancer were: men 43.6/100 000 per year; women 27.9/100 000 per year. The rates for gastric cancer were: men 36.7/100 000 per year, women 9.9/100 000 per annum. These figures were three to six times higher than those recorded by cancer registries in Bangalore, Madras, and Bombay. The incidence rates for oesophageal and gastric cancer in Islamabad (southern district of Kashmir) were 4.1 to 5.4 times higher in men and 1.5 to 2.0 times higher in women than those for Kupwara (northern district of Kashmir). The incidence rates for oesophageal and gastric cancer in Muslims, Hindus, and Sikhs were different. The epidemiology of oesophageal cancer in Kashmir was similar to that found in the 'Asian oesophageal cancer belt'. At the same time Kashmir also had an unprecedented high incidence of gastric cancer. Kashmiries have special personal and dietary habits. Further studies are needed to define the relation between these habits and the occurrence of oesophageal and gastric cancer.

The incidence of oesophageal cancer in the United States is low. The age standardised incidence rates/100 000 per year are 6.0 in men and 1.6 in women.<sup>1</sup> The age standardised incidence rates in Europe are 7.1 in men and 1.0 in women.<sup>2</sup> These data are by no means representative of the incidence rates for this disease throughout the world. High incidence rates for oesophageal cancer have been reported from the Caspian littoral of Iran, the Henan and Shanxi provinces of China, and in the Homeland state of Transkei in South Africa.<sup>3-5</sup> Each of these areas has regional peculiarities that are probably of aetiological importance.

Gastric cancer is the sixth most common cause of cancer death in the United States, but although it still remains a major health problem there, the number of deaths from this disease have decreased considerably in both men and women over the past 40 years.<sup>6</sup> In contrast, the incidence rate is high in Japan and Chile.<sup>7</sup> Migrants from high to low incidence countries show a significant decrease in disease occurrence

suggesting that the cause is related to environmental factors.

It has been suggested from clinical experience that oesophageal and gastric cancer are very prevalent in Kashmir but there are no population based data available on incidence. The present study was conducted to determine the incidence of oesophageal and gastric cancer in Kashmir.

## Methods

### DEMOGRAPHY OF KASHMIR

Kashmir is one of the three provinces (Kashmir, Jammu, and Ladakh) of the Jammu and Kashmir State (India). Kashmir valley is situated at a height of 1800-2400 m above sea level and divided into six districts. The population of the valley that was studied was 2 899 587 (1 547 262 men; 1 352 325 women).<sup>8</sup> Kashmir has a non-migrant population who have special social, personal, and dietary habits. Although all the residents have a common ethnic origin, the habits of Muslims (94.5%), Hindus (4.2%), and Sikhs (1.1%) are different.<sup>9</sup>

### PERSONAL AND DIETARY HABITS

Alcohol is not consumed by the Muslim population for religious reasons, while alcohol consumption is common in male Sikhs. Hindus, by and large, do not drink it. Smoking is very common in Muslim and Hindu men while Sikhs do not smoke because of religious beliefs. The most common form of smoking is the hubble bubble (hukkha) whereby the smoke is inhaled after it has passed through water placed in an earthen container. Addiction to drugs such as opium is non-existent. Snuff is often used by Muslims.

Salted tea is the most popular and common drink of Muslims. The method of preparation is typical and practised exclusively in this region. Green tea leaves (not grown in Kashmir) are brewed in sodium bicarbonate until a thick red brown coloured extract is obtained. The extract is then diluted with water and salt and milk are added. The tea is repeatedly boiled in a samawar and drunk while boiling hot. The daily consumption per head is quite large (approximately up to 10 cups a day).

Special green tea (kehwa), prepared by boiling green tea in cardamom, cinnamon, and saffron is consumed in moderation (approximately two to four cups a day) by Hindus.

North Kashmir (Kupwara and Baramulla) is one of the highest fruit producing regions in India and local inhabitants have an adequate intake of locally grown fruit.

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Accepted for publication  
15 April 1991

The staple diet of all communities is boiled rice (batta) and boiled cruciferous leafy vegetable of the *Brassica oleracea* locally known as haak. Almost all the population is meat eating and consumes sufficient lamb.

Other special food items consumed by the people are: dried and pickled vegetables, sun dried and smoked fish, mixed spice cake (wur), and vegetable food colourants (*Celosia argentea* - mawal; saffron - zafran). In addition to the food items described, there is a large consumption of locally grown vegetables, red chillies, and lotus stem.

#### STUDY DESIGNS

The study period was from 1 July 1986 to 30 June 1989. All newly diagnosed and histologically proved cases of oesophageal and gastric cancer were prospectively recorded. All possible sources of assessing, investigating, and treating these patients were approached to record details. The patients' details were carefully assessed to avoid double registration of any one patient. The information collected included age, sex, presenting symptoms, radiological and endoscopic features, histological report of biopsy material, surgical findings, and histological report of the resected specimens.

The various formulas used to calculate the incidence of oesophageal and gastric cancer were as follows<sup>10</sup>:

(1) The crude incidence rate (CR) was defined

as an estimate of the number of new cancer cases/100 000 population at risk per year.

$$CR = \frac{\text{New cancer cases in 1 year}}{\text{Total population at risk in 1 year}} \times 100\,000$$

(2) The age specific rate (ASR) refers to the number of cases of cancer among individuals in each specific age category (five-year age group)/100 000 per year.

$$ASR = \frac{\text{New cases in a particular age group in 1 year}}{\text{Population in that age group in 1 year}} \times 100\,000$$

(3) The age standardised incidence rate (ASIR) is the rate that would have occurred if the observed age specific rate had operated in a standard world population age structure. The number of individuals in each age group (five-year age group) in a standard world population was multiplied by the corresponding incidence rate observed to obtain the number of cases that would have been expected to occur in one year in a standard world population. The expected numbers were added and the sum obtained was divided by the total number of individuals in the standard population to give the age standardised incidence rate.

(4) The truncated age adjusted incidence rate (TR) is an age standardised incidence rate in which data are restricted to the age range 35 to 64 years and each five-year age group within it is given the weight appropriate to the standard world population.

TABLE I Age specific incidence rate, crude incidence rate (CR), age standardised incidence rate (ASIR), and truncated age (35-64 years) adjusted incidence rate (TR) for oesophageal and gastric cancers in Kashmir 1986-9. All numbers are new cancer cases/100 000 population at risk per year

Age group (yrs)	Oesophageal cancer		Gastric cancer	
	Men	Women	Men	Women
20-24	1.6	0	0	0.9
25-29	1.6	0	0	0
30-34	7.7	7.3	1.9	1.1
35-39	22.4	21.3	10.7	4.5
40-44	39.5	46.0	44.9	19.4
45-49	129.0	51.0	58.3	12.7
50-54	178.6	108.5	106.7	62.0
55-59	121.5	31.1	106.9	31.1
60-64	198.4	92.9	238.1	37.1
65-69	136.5	154.6	198.5	15.4
70-74	194.8	248.6	177.1	0
75-79	49.5	61.9	99.0	0
80	20.7	0	62.1	0
CR	22.6	11.5	17.0	4.3
ASIR	42.6	27.5	36.7	9.9
TR	108.2	70.0	83.8	31.9

#### Results

During the three year period, 1515 cases of oesophageal cancer (1050 men and 465 women) and 966 cases of gastric cancer (789 men and 177 women) were registered. Seven patients had the two cancers simultaneously - oesophageal cancer of the squamous cell variety and gastric cancer of the adenocarcinoma type at two different sites. One patient had simultaneous gastric adenocarcinoma and ampullary adenocarcinoma. The mean (SD) ages of occurrence for oesophageal cancer and gastric cancer were 52.0 (5.5) years and 55.0 (7.5) years respectively. The male to female ratio for oesophageal cancer was 1.5:1 and that for gastric cancer was 4.7:1. Oesophageal cancer was of the squamous cell variety in 1293 (85.3%) patients, adenocarcinoma in 220 (14.6%), and leiomyosarcoma in two. Oesophageal tumours in which histology showed adenocarcinoma were limited to the oesophageal lumen and had not affected the cardia or fundal region of stomach.

TABLE II Crude incidence rate (CR), age standardised incidence rate (ASIR), and truncated age (35-64 years) adjusted incidence rate (TR) of oesophageal and gastric cancer in six districts of Kashmir 1986-9. All numbers are new cancer cases/100 000 population at risk per year

	Islamabad (north Kashmir)		Pulwama		Budgam		Srinagar		Baramulla		Kupwara (south Kashmir)	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Oesophageal cancer:												
CR	30.5	12.2	20.6	12.0	14.3	9.8	27.8	12.7	22.6	11.2	8.6	8.4
ASIR	70.0	25.0	42.0	25.0	29.0	20.0	54.5	26.2	44.5	23.0	17.0	16.0
TR	150.0	65.0	105.0	60.0	58.2	50.2	138.0	65.0	108.5	54.0	38.2	40.0
Gastric cancer:												
CR	28.6	4.8	15.0	4.1	13.8	4.6	22.8	5.4	9.7	3.5	5.7	2.5
ASIR	60.0	10.0	30.0	9.0	27.0	8.0	45.0	11.0	20.0	7.0	11.0	5.0
TR	145.2	24.0	75.0	21.0	68.0	25.0	116.0	28.0	49.0	18.0	27.0	13.0

TABLE III Crude incidence rate (CR), age standardised incidence rate (ASIR), and truncated age (35-64 years) adjusted incidence rate (TR) of oesophageal and gastric cancer in Muslims, Hindus, and Sikhs of Kashmir 1986-9. All numbers are new cancer cases/100 000 of population at risk per year

	Muslims		Hindus		Sikhs	
	Men	Women	Men	Women	Men	Women
Oesophageal cancer						
CR	23.2	11.6	10.6	5.2	28.2	12.9
ASIR	46.2	25.0	23.0	11.0	59.0	26.0
TR	120.0	57.0	55.0	25.0	145.0	65.0
Gastric cancer						
CR	17.4	4.4	12.1	3.4	0	0
ASIR	37.0	11.0	25.0	8.0	0	0
TR	89.0	23.0	64.0	18.0	0	0

Those tumours affecting the stomach and extending to the oesophageal lumen were considered gastric cancers. Gastric cancer was reported as adenocarcinoma in 960 patients, gastric lymphoma in four, and leiomyosarcoma in two. Oesophageal cancer occurred in upper third of the oesophagus in 27 (1.8%) patients, the middle third in 916 (60.4%), and the lower third in 572 (37.8%). Gastric cancer was situated in the cardiac region in 132 (13.7%) patients, in the body of stomach in 375 (38.8%), and in antrum in 459 (47.5%).

The CR, ASR, ASIR, and TR for oesophago-gastric cancer are shown in Table I. The CR, ASIR, and TR for oesophago-gastric cancer in the various districts is given in Table II. Incidence rates for oesophageal and gastric cancer were highest in the southern district (Islamabad) and lowest in northern district (Kupwara) of Kashmir. The incidence rates for central districts (Srinagar, Badgam) were intermediate. The ASIR for oesophageal cancer in men from Islamabad was 4.1 times higher than that in men from Kupwara, 150 km away. However, the ASIR for oesophageal cancer in women was only 1.5 times higher in Islamabad compared with Kupwara. Similarly, the ASIRs for gastric cancer in men and women from Islamabad were 5.4 and 2.0 times higher respectively than those from Kupwara. The CR, ASIR, and TR for oesophago-gastric cancer in Muslims, Hindus, and Sikhs are given in Table III. Incidence rates for oesophageal cancer were high in Muslims and Sikhs and low in Hindus. However, no case of gastric cancer was recorded in Sikhs in the study period while the incidence rate for gastric cancer in Muslims was higher than that in Hindus.

### Discussion

This study on the incidence of oesophago-gastric cancer was conducted in a population that is non-migratory, and patients invariably report to the District Medical Centre, Medical College Hospital, Institute of Medical Sciences, and private clinics and hospitals in the valley. The acceptability of allopathic treatment in the general public is high and there are no alternative therapies such as homeopathy and ayurvedic. The public is aware of oesophago-gastric cancer and demands endoscopic and histological proof of the disease. There is a network of investigative laboratories at district and subdistrict level and a good referral system exists between these health centres and the specialist institutions primarily involved in treating this disorder. In defining the

incidence of oesophago-gastric cancer, we registered only histologically documented cancer cases. This may have underestimated the incidence for the following reasons:

(a) Not all patients with cancer may have access to a doctor. Because of this we studied only those populations that lived in areas of the valley that were accessible throughout the year;

(b) Clinicians may not ask for additional endoscopic and histological proof of cancer when the diagnosis is obvious from clinical or radiological studies. When we asked doctors about this we were assured that both they and the patient or their family demand endoscopic and histological proof of suspected oesophago-gastric cancer;

(c) Patients with histological proof of malignancy from metastatic deposits may not be investigated for a primary tumour in the oesophagus or stomach. In view of the high prevalence of oesophago-gastric cancer in Kashmir, however, it is the practice of clinicians to screen all patients with metastatic disease for a primary tumour in the oesophagus and stomach by upper gastrointestinal endoscopy. An alternative would be to undertake radiological studies of the upper gastrointestinal tract as the diagnostic criteria of oesophago-gastric cancer. The main difficulty is the poor quality of barium meal examination and its high false negative rate in patients with histologically documented upper gastrointestinal cancer.

In India, most of the data on the epidemiology of oesophago-gastric cancer have been obtained from hospitals and are mostly related to inpatient admissions.<sup>11,12</sup> Lately, population based cancer registries have been set up at Bombay, Bangalore, and Madras under the auspices of the National Cancer Registry, Indian Council of Medical Research.<sup>13</sup> A comparative assessment of the present data with those from these cancer registries shows that the incidence of oesophago-gastric cancer is three to six times higher in Kashmir (Table IV).

The incidence of oesophageal cancer in men showed noticeable differences across the 150 km of the Kashmir valley. The ASIR was 70.0 in men from Islamabad district and 17.0 in men from Kupwara. Oesophageal cancer exhibits dramatic differences in prevalence over relatively short geographical distances. Thus, along the few hundred miles of the Caspian littoral of Iran there is a 20 fold variation in the death rate from oesophageal cancer, and in north China the oesophageal cancer death rate is 100 times higher in the Linhsien area than in the lowest risk area.<sup>3,4</sup> In contrast, however, to these figures from Iran and China, the incidence of

TABLE IV Comparison of age standardised incidence rates for oesophageal and gastric cancer from Bangalore, Madras, Bombay, and Kashmir

	Oesophageal cancer		Gastric cancer	
	Men	Women	Men	Women
Bangalore*	6.6	5.3	10.6	6.2
Madras*	8.8	6.0	17.6	7.4
Bombay*	11.4	8.9	5.9	4.7
Kashmir†	42.6	27.9	36.7	9.9

\*Data from the National cancer registry, ICMR, New Delhi 1988.<sup>11</sup>

†Data from the present study.

oesophageal cancer in women in Kashmir did not show a correspondingly high regional variation. A regional variation similar to that for oesophageal cancer was observed for gastric cancer in men from Kashmir. The prevalence of gastric cancer in high risk areas has not shown such wide variations.

In regions of the world with high incidences of oesophageal and gastric cancer, extensive studies have failed to identify specific aetiological factors. These studies have, however, strengthened the view that food habits and lifestyle are closely associated with a high incidence of oesophagogastric cancer.<sup>3-5,9,12</sup> In Kashmir, the most important specific food habit is consumption of large quantities of hot salted tea. The use of sodium bicarbonate at the time of boiling the tea leaves and the further addition of common salt to the prepared tea cause one to suspect that the tea does more than cause thermal injury to oesophageal epithelium. Common salt (NaCl) is a well known irritant of gastric epithelium and has been considered a risk factor for gastric cancer.<sup>14</sup> Another specific dietary habit in Kashmir is the practice of drying raw food stuffs in open sun under humid conditions.<sup>9</sup> These foods contained significant amounts of N-nitroso compounds.<sup>15</sup> In addition, analytical studies of other Kashmiri foods indicate the possibility of substantial exposure to N-nitroso compounds, from exogenous as well as endogenous dietary sources.<sup>16</sup> The dietary items containing substantial amounts of N-nitroso compounds include: salt tea, dried fish, vegetables especially *Brassica oleracea* (haak), red chillies, and spice cake (wur).<sup>17</sup> In addition, salt tea showed the formation of high amounts of N-nitrosopipercolic acid with several unidentified non-volatile N-nitroso compounds on nitrosation of tea extracts under conditions simulating the fasting human stomach.<sup>18</sup>

Perhaps the area of the world with the highest incidence of oesophageal cancer is in Iran and the Soviet Union around the Caspian Sea (Table V).<sup>3</sup> An oesophageal cancer belt extends across Asia from the southern shore of the Caspian Sea in Iran, through Soviet Central Asia and Mongolia to northern China.<sup>19</sup> The Kashmir valley borders this belt on the southern side and the epidemiology of oesophageal cancer has many peculiarities common to this belt. The occurrence of chronic oesophagitis in the general population is high in this belt and we recently documented a prevalence of chronic oesophagitis in 74.7% and dysplasia in 7.5% of 107 healthy volunteers from Kashmir.<sup>20</sup> In addition, however, Kashmir has an unprecedented high incidence of gastric carcinoma (Table VI). The gastric cancers in Kashmir are of the intestinal type in 80.4% of cases and of the diffuse variety in 17.8%, as assessed by Lauren's classification (personal observation). The intestinal type of gastric cancer is prevalent in high risk areas and is considered to be caused by environmental factors. A significant number of patients had simultaneous oesophageal and gastric carcinoma. This points to the fact that the population is exposed to such carcinogens which predispose to both esophageal as well as gastric cancer.

The incidence of oesophagogastric cancer in

TABLE V Comparison of geographical differences in age standardised incidence rates for oesophageal cancer from Iran, USSR, and Kashmir

	Oesophageal cancer		M:W
	Men	Women	
Iran*:			
Gonabad	93.1	110.0	0.8:1
Gorgan	66.6	49.2	1.3:1
Gilan	20.1	6.2	3.2:1
USSR†:			
Turkemenia	51.1	33.2	1.5:1
Kazakhstan	47.8	26.3	1.8:1
Uzbekistan	28.5	13.7	2.0:1
Kashmir‡:			
Islamabad	70.0	25.0	2.8:1
Srinagar	54.5	26.2	2.0:1
Kupwara	17.0	16.0	1.0:1

\*Data from reference.<sup>3</sup>

†Data from reference.<sup>7</sup>

‡Data from present study.

TABLE VI Comparison of age standardised incidence rates for gastric carcinoma from Japan, USA, and Kashmir

	Gastric cancer		M:W
	Men	Women	
Japan*:			
Nagasaki	100.2	51.0	1.9:1
Miyagi	88.0	42.0	2.0:1
Osaka	78.0	38.5	2.0:1
Fukuoka	75.0	38.4	1.9:1
USA†:			
Blacks	22.4	9.1	2.4:1
Whites	7.5	3.5	2.1:1
Japanese	34.3	15.6	2.1:1
Chinese	9.0	4.5	2.0:1
Kashmir‡:			
Islamabad	60.0	10.0	6.0:1
Srinagar	45.0	11.0	4.0:1
Kupwara	11.0	5.0	2.2:1

\*Data from reference.<sup>7</sup>

†Data from reference.<sup>6</sup>

‡Data from present study.

Muslim, Hindu, and Sikh populations showed significant differences. Of importance was the fact that Sikhs had the highest incidence of oesophageal cancer but no gastric cancer was recorded over the period of study. These differences could be related to the different personal and food habits of these religious groups and need further study. The geographical differences in the incidence of oesophagogastric cancer in the various districts is more difficult to explain. North Kashmir has a high production and consumption of fresh fruits and this may be the cause of the low incidence of oesophagogastric cancer in these districts. Other factors like zinc and molybdenum deficiency may explain these regional differences.<sup>21</sup>

We believe Kashmir is a high risk area for oesophageal cancer, similar to and in continuity with the 'Asian oesophageal cancer belt'. In addition, the occurrence of a high incidence of gastric cancer in Kashmir is unprecedented. The special personal and dietary habits of the population are the most likely aetiological factors. Further studies are needed to find a correlation between various possible aetiological factors and the occurrence of these cancers.

The authors thank Mr Mehraj-ud-Din, for secretarial assistance.

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