

# Dietary intake and nutritional status of patients with gall bladder cancer

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## Abstracts

Gall Bladder Cancer (GBC) is common in northeastern Indian states. Industrial pollutants, lifestyles, dietary habits, gallstones, socio-economic status etc. have been proposed, but, none of them explain the incidents of GBC. With an objective to study the dietary pattern, nutritional status, lifestyle and non dietary habits a closed ended questionnaire was used to interview GBC patients taking treatment in Tata Memorial Hospital, India. More women than men had GBC with an male to female ratio of 1:3.6. One third, patients were from low socio economic group. 33.32% patients were overweight. Dietary habits revealed a high risk associated with less consumption of vegetables and fruits. 68.9% patients were using mustard oil as cooking medium. 76.5% patients had past history of gallstones. Malnutrition, Low socio-economic status, decreased Micronutrients in the diet, use of adulterated mustard oil and consumption of fishes from contaminated water sources may be influencing the incidents of GBC.

**Keywords:** Gall Bladder Cancer, Nutrition, Lifestyle

## Introduction

Gall Bladder cancer (GBC) in India is one of the common entities among Gastro Intestinal (GI) tract cancers (Batra et al. 2005). Worldwide Incidence of GBC varies from 27/100000 in Chile to 1/100000 in United States. In India, as per the data available with the National Cancer Registry (1992) the incidence varied from 10 per 100000 in Delhi to 2-3 per 100000 in the South. Population based data indicates that the incidence of GBC in women is

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higher in northern Indian cities (5-7 per 100000) and lowest (0-0.7 per 100000) in southern India (Pandey et al. 2002). Dhir et al. in 1999 reported that the GBC is more common in northern states like Uttar Pradesh, Bihar, Orissa, west Bengal and Assam as compared to southern states of India. As per the above studies the distribution suggested geographical, ethnic differentials, cultural variations and major environmental factors may influence GBC incidence. (Ramkumar et al. 2006, Tyagi et al. 2008). Number of factors has been proposed to explain etiology of GBC. Urbanization, industrialization, Life style changes, faulty dietary habits and ageing all are reported to contribute for epidemiological changes in our country (Chaurasia et al. 1999, Murthy et al. 2004).

Obesity has been proposed as a major risk along with high intake of calorie. High carbohydrate and oil rich foods have contributed to Gall Bladder Cancer incidences (Zatonski et al.1992). There are various factors which are known to promote Malnutrition in cancer patients. Malnutrition has direct impact on the quality of life thus reducing the survival rate. (Nitenberg et al. 2000).

Most of the epidemiological studies conducted worldwide, suggest that some dietary factors influence development of Gall Bladder Cancer (GBC). Also, ecological evidence indicates considerable geographic variation. (Ramkumar et al. 2006). Strom et al. in 1995 proposed chronic infections like Typhoid carrier state or Helicobacter infections, lipid peroxidation, genetic susceptibility as some of the risk factors promoting GBC.

Many factors in diet have also been attributed to be either causative or protective in Gall Bladder Cancer (GBC). In a study conducted by Zatonski et al. in 1992 found that Vegetables and fruits have a protective effect. It was also observed that, GBC had inverse association with fiber intake, vitamin C and vitamin E. There are very few studies which explain the relation between diet and GBC from India. Hence the present study was undertaken to obtain information on diet, Life style, nutrient intakes and nutritional status of GBC patients.

## Materials and methods

However the variations in Gall Bladder Cancer (GBC) incidence of different populations might be partly determined by their geographical, ethnic differentials, cultural variations, major environmental influences and dietary habits. This was an observational retrospective study. 96 patients suffering from GBC were selected from the Out Patient and In Patient departments of Tata Memorial Hospital, Mumbai, India. Data was collected using a close end questionnaire to obtain information on demographic characteristics, medical history and lifestyle factors. Non dietary habits such as smoking, alcohol and tobacco consumption were recorded. A food frequency questionnaire (FFQ) was used to obtain information about frequency of consumption of cereals, pulses, vegetables, fruits, non vegetarian foods, milk products, nuts and oil seeds, fried foods, sweets and beverages. Three day dietary recall was taken to assess the daily nutrient consumption.

Anthropometric measurements i.e. height and weight were recorded and their body mass index was calculated by using the formula.

$$BMI \approx \frac{\text{Weight in Kgs}}{\text{Height in m}^2}$$

To know Clinical status Laboratory reports such as Complete Blood Count, Hemoglobin, WBC, Platelets reports at the time of admission were recorded.

The Subjective Global Assessment (SGA) is a clinical technique that combines data from history such as weight change, dietary intake change, GI symptoms, and changes in functional capacity too physical examination such as loss of subcutaneous fat, muscle wasting, ankle or sacral edema and ascites.

Data was analyzed by using SPSS Version-20. Descriptive statistics like mean, standard deviation, percentage etc. was computed for data presentation.

## Results and discussion

Women are two to six times more commonly affected by Gall Bladder cancer (GBC) than men (Scott et al. 1999). Female-to-male incidence ratios were generally around 3, but ranged from 1 in Far East Asia to over 5 in Spain and Colombia (Randi et al. 2006.)

A substantial female predominance exists worldwide, with female-to-male ratios of approximately 2.5:1 to 3:1. GBC is the most common cancer affecting women in Chile. (Schottenfeld et al. 2006). Female to male ratio is even high in those areas where the GB disease and GBC is rare as in Uganda (Rizvi et al. 2003). Bushra et al. in a study conducted in 2010 found that in a total of 153 GBC patients, 88.23% (135 patients) were females as compared to 11.77% (18 patients) males. The ratio was 2.5:1 in an Italian study. Findings in the present study are in agreement with reports in the literature. Among the subjects included in this retrospective study, 22.9% ( $n=22$ ) were men and 77.1% ( $n=84$ ) were women. The male to female ratio was 1:3.6.

Most studies have reported higher incidence of Gall Bladder Cancer (GBC) between 6<sup>th</sup> and 7<sup>th</sup> decades of life and it rises with age. (Rizvi et al. 2003). Schottenfeld et al. in 2006 observed that it is most typically diagnosed in the seventh decade of life, with a median age of 62-66 years. In 2010, Bushra et al. found

that most of the patients were older than 30 years of age and incidence in males peaked after the age of 60 years and after 40 years in females.

In the present study most of the patients were older than 40 years of age. Among males the youngest was 30 yrs and oldest was 75 years of age, with a mean of 52 years. Among females, the youngest patient was 25 years and the oldest was 80 years of age, with a mean age of 56 years.

In India, Gall Bladder cancer (GBC) shows varying geographic distribution, as the incidence is much higher in Delhi as compared to South India. Detailed analysis shows an increasing trend in the incidence rate of this cancer in the urban population of Delhi. (National Cancer Registry, 2001). Bharbhuiya et al. in 2009 carried out a retrospective study at the Cancer Hospital and Research Institute, Gwalior, Madhya Pradesh. They- reported that most of the patients admitted were residents of north Madhya Pradesh, adjoining Uttar Pradesh and Rajasthan.

In the present study it was observed that 80% ( $n= 77$ ) of the patients were from North India. The incidence of GBC was highest in Uttar Pradesh (36%,  $n=34$ ) followed by Bihar (16%,  $n=15$ ) 15% of the ( $n=14$ ) patients belonged to Maharashtra and West Bengal each (Table No. 1)

Table 1 : Regional distribution of GBC patients

Region	Frequency	Percent
Maharashtra	14	14.6
Uttar Pradesh	33	36.1
Jharkhand	6	6.3
Uttaranchal	2	2.1
Madhya Pradesh	3	3.1
Orissa	2	2.1
Bihar	15	16.2
West Bengal	17	18.1
Assam	1	1.0
Bangladesh	1	1.0
Nepal	1	1.0
Total	96	100

Lower socioeconomic status may be associated with delayed access to cholecystectomy for gallstones, which may increase GBC rates. A study conducted by Dutta et al. in 2005 found that a significant proportion of Indian patients were from low socioeconomic status. Both genetic factors and socioeconomic issues that delay or prevent access to cholecystectomy for gallstones are thought to be contributory. (Randi et al. 2009)

In the present study, the subjects selected were from mixed socio economic background. One third (33.3%), ( $n =32$ ) of patients were from low income group and 54.2% ( $n =52$ ) patients were from lower middle income group, 5.2% ( $n=5$ ) from higher middle income group and 7.3 % ( $n =7$ ) from higher income group. Thus, 87.5% ( $n=84$ ) of total number of patients belonged to the lower socio economic group (Table No. 2)

Table 2 : Socio economic status of GBC patients

Income Level	Frequency	Percent
Low Income	32	33.3
Lower Middle Income	52	54.2
High Middle Income	5	5.2
High Income	7	7.3
Total	96	100

Renard et al. in 1987 observed that the incidence of Gall Bladder Cancer (GBC) was similar in urban and rural areas. Similarly in the present study 52.1% ( $n=50$ ) lived in rural areas and 47.9% ( $n=46$ ) came from urban areas.

In a study conducted by Enriqueta et al. in 2010, risk of GBC was found to have an inverse linear correlation with years of education in both sexes, although it was more significant for women. The risk differential from low to high schooling was 1.98 among men and 6.43 among women. However in the higher education group, the risk was the same for women and men.

In the present study, 67.8% (n=65) of the patients had received primary schooling upto 4<sup>th</sup> standard, 17.7% (n=17) of patients had done their schooling till SSC, 13.5% (n=13) were graduates and one patient had completed post graduation (Table No. 3)

Table 3 : Literacy level of GBC patients

Education	Frequency	Percent
Illiterate	18	18.8
Primary	47	49
SSC	17	17.7
Graduate and above	14	14.5
Total	96	100

Rizvi et al. in 2003, reported an increase in risk of GBC as there was an increase in the age at menarche but the association was not statistically significant. However, there is not much information in the literature regarding reproductive history. In the present study, it was observed that the percentage of menopausal women 42.7% (n=41) having GBC was higher than the percentage of menstruating women 34.4% (n=33).

The history of past/present illness was recorded. Patients were asked whether they had suffered from typhoid, diabetes, cholelithiasis, hypertension, hysterectomy and/or had a family history of cancer. Also, women were asked whether they had undergone hysterectomy. The data revealed that only 11.5% (n=11) patients had hypertension prior to detection of GBC.

People with diabetes generally have high levels of triglycerides. Fatty acids may increase the risk of gallstones. In the present study, only 11.5% (n=11) had diabetes mellitus. Only 5.4% (n=4) patients had a past history of hysterectomy, whereas 94.6% (n=74) female patients had no previous gallbladder disease history.

Hsing et al. in 2006 found that typhoid contributed significantly to the risk of GBC in Chile. Chile has been a highly endemic area for typhoid fever since 1950, with an annual incidence rate of about 60 per 100,000 person-years until 1976. (Roa et al. 2004). This report is consistent with previous reports suggesting a link between chronic typhoid carriage and GBC in typhoid-endemic area, such as India.

In contrast to the above studies, in the present study only one patient had a past history of typhoid fever. Some patients may have had typhoid in the past but were not able to identify the type of fever.

Studies show that persons with a first degree relative (parent, brother or sister) with Gall Bladder Cancer (GBC) are five times more likely to develop GBC than those who do not have a relative with it. (Malin et al. 2002).

Ramkumar et al. in 2006, reported the results of a retrospective study on 328 histologically proven cases of Gall Bladder Cancer (GBC) and an equal number of controls with gall stone disease, attending the Department of Surgical Oncology, Institute of Medical Sciences, Banaras Hindu University from January 1999 to November 2004. The study participants were clinically

examined and the demographic data was assessed. The investigators found that there was a significant greater risk of GBC with family history of Gall Bladder (GB) disease, GB stones and GBC.

However in the present study only 2.1% (n=2) patients had a family history of cancer. The symptoms of Gall Bladder (GB) disease are not always obvious, and many patients may in fact experience no symptoms at all. Symptoms of GB stones in women can sometimes be mistaken for premenstrual cramps. The primary symptom of GB inflammation and pain is often referred to as biliary colic. The main diseased GB symptom is acute or intermittent pain in the abdomen. Indigestion, gas, a feeling of fullness after meals, constipation, and nausea are the other usual symptoms. Other GB symptoms include intolerance to fats, dizziness, jaundice, anemia, acne, and other lesions.

Among the 96 patients included in the present study 72.9% (n=70) had abdominal pain. In the present study only 8.3% (n=8) patients complained of nausea and/or vomiting. The Fox Chase Cancer Center reports that jaundice is one of the possible signs that a patient is suffering from Gall Bladder Cancer (GBC). The Johns Hopkin's Pathology reports indicate that almost 90 percent of patients suffering from GBC experience this symptom (Pritchard et al. 2011). In the present study a positive association of Jaundice as a symptom of GBC was observed with, 79.2% (n=76) patients reported, that they had jaundice close to the time of diagnosis. The data revealed that 9.4% (n=9) had pallor, 11.5% (n=11) complained of icterus and 8.3% (n=8) patients had anorexia (Table No 4)

Table 4 : Symptoms exhibited by GBC patients

Symptoms	Frequency	Percent
Jaundice	76	77.6
Pain In Abdomen	70	72.9
Gall stones	71	71.9
Ascitis	5	5.2
Nausea / Vomiting	8	8.3
Edema	2	2
Anorexia	8	8.3
Pallor	9	9.4
Icterus	11	11.6
Anemia	89	93
Platelets	22	22.6

The presence of gallstones increases the risk of Gall Bladder Cancer (GBC) 4- to 5-fold. (Bernstein et al. 2001). Results of the present study are in agreement with previous reports, as a majority of patients 71.9% (n=70) had cholelithiasis in the past or in the present.

Anemia is common in cancer patients, and the result is that less oxygen is delivered to the tumor, that is, hypoxia occurs. A low-oxygen environment (hypoxia) promotes tumor growth. A study was conducted by Caro et al. in 2001 to systematically review and obtain an estimate of the effect of anemia on the survival of cancer patients. These authors found that the increased risk of mortality in cancer patients who were anemic was as high as 65%. In the present study the mean hemoglobin of males was 11.23g/dL with minimum hemoglobin being 6.85 g/dL and maximum was 15.3 g/dL. Mean hemoglobin of females was 11.03 g/dL with minimum being 7.1 g/dL and maximum was 13.3 g/dL. (Table No. 4) The acceptable range of hemoglobin is 11.0 g/dL to 15.0 g/dL. Almost all 93% (n=89) patients were anemic. Majority of the patients, 74% (n=68) had a WBC count within acceptable range (150-400 x10e9/L). The platelet count of, 23% (n=22) patient's was below 150x10e9/L.

Reduced physical activity heightens the risk of gallstone disease whereas increased physical activity helps prevent cholelithiasis, (Leitzmann et al. 1999). The activity level, or the lifestyle of individuals may have some impact on Gall Bladder Cancer events. A majority (66.6%, n=64) of patients were moderately active, 24% (n=23) were in the heavy worker category and only 9.4% (n=9) patients were leading a sedentary lifestyle.

Only a few studies have examined the relationship between cigarette smoking and Gall Bladder Cancer (GBC), and the findings have been inconsistent. A study conducted by Shukla et al. in 2008 has shown a positive association between smoking and GBC.

A population based case-control study on 333 gallbladder incident cases was carried out in Delhi by Tyagi et al. in 2009, to identify the risk factors. Cases were matched with two controls based on age ( $\pm 5$  years), sex and marital status (in case of females). They found that smoking and alcohol consumption increased the risk of Cancer of gall bladder. The risk among those who smoked cigarettes (OR=3.05, CI=1.33-6.98) was higher than that seen among bidi smokers (OR=2.25, CI=1.38-3.69). However, the present study did not show any significant association, since only 10.4% (n=10) of the patients smoked.

In 2008, Shukla et al. conducted a prospective case-control study involving 78 newly-diagnosed cases of Gall Bladder Cancer (GBC) and 78 age- and gender-matched controls with cholelithiasis. All participants were asked about their lifestyle history, with an emphasis on habits with chewing betel nut and tobacco, alcohol consumption and smoking. The investigators reported the GBC was common among tobacco chewers. In the present study only 8.3% (n=8) patients were found to be habitual tobacco chewers. Among the 8 patients who consumed tobacco products, three consumed gutka, three consumed paan with tobacco, and two chewed tobacco.

Yagy et al. in 2008 conducted a prospective study to evaluate the association of smoking and alcohol consumption with the risk of Gall Bladder Cancer (GBC). They found that there was no clear association between alcohol consumption and GBC. Among the 96 patients in the present study, only 12.5% (n=12) of patients stated that they consumed alcohol.

It is not clear if exposure to certain chemicals in the workplace or the environment increases the risk of Gall Bladder Cancer (GBC). Studies in laboratory animals suggest that nitrosamines may increase the risk of GBC. Workers in the rubber and textile industries, automobile, wood-finishing, oil, paper, chemical, textile, shoe, fiber and metal-fabricating industries may have more GBC than the general public (Rajgopalan et al. 2004). In the present study, seven patients were industrial workers and a little more than one fourth patients were farmers. (Figure 1). A considerable proportion of women patients (41.7%, n=40) worked in offices and one patient was a laborer.

The regions of Eastern Uttar Pradesh and Western Bihar where Gall Bladder Cancer (GBC) is highly prevalent lie downstream of the river Ganges which is the main source of drinking and irrigation water. It also receives untreated domestic sewage and industrial effluents and it is possible that certain environmental pollutants may act as carcinogens. (Pandey et al. 2002). Occupational exposure in the rubber, automobile, wood-finishing, oil, paper, chemical, textile, shoe, fiber and metal-fabricating industries lead to increased risk (Lazcano et al. 2001).

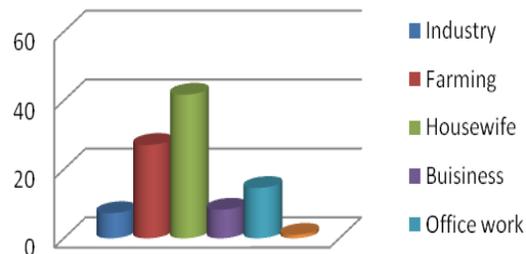


Figure 1 : Occupation profile of patients

The above Figure 1 shows that, 45.8% (n=44) worked in dusty environment, one patient worked in chemical factory and a little more than half 53.1%, (n=51) were housewives. Hence association with environmental exposure cannot be commented upon.

The BMI of individuals has been classified by WHO indicating degree of underweight (Table 5). BMI has been directly related to health risks and death rates in many populations (Larsson et al. 2001).

Table 5: WHO's International Classification of adult underweight, overweight and obesity according to BMI

Classification	BMI(kg/m <sup>2</sup> )		Observed Value	
	Principal cut-off zpoints	Additional cut-off points	Frequency	Percent
Underweight	<18.50	<18.50		
Severe thinness	<16.00	<16.00	3	3.1
Moderate thinness	16.00 - 16.99	16.00 - 16.99	2	2.1
Mild thinness	17.00 - 18.49	17.00 - 18.49	3	3.1
Normal range	18.50 - 24.99	18.50 - 22.99 23.00 - 24.99	42	43.8
Overweight	$\geq 25.00$	$\geq 25.00$		
Pre-obese	25.00 - 29.99	25.00 - 27.49 27.50 - 29.99	17	17.7
Obese	$\geq 30.00$	$\geq 30.00$		
Obese class I	30.00 - 34.99	30.00 - 32.49 32.50 - 34.99	10	10.4
Obese class II	35.00 - 39.99	35.00 - 37.49 37.50 - 39.99	1	1
Obese class III	$\geq 40.00$	$\geq 40.00$	2	2.1
Total			96	100

Source: Adapted from WHO, 1995, WHO, 2000 & WHO 2004.

Obesity increases the risk for gallstones, and thus may be a risk factor of Gall Bladder Cancer (GBC). A meta analysis study by Larsson et al. in 2007 indicated that the risk of GBC increased with increasing BMI. Risk was 15% and 66% higher among those who were overweight and obese, respectively, as compared with those of normal weight. The association between obesity and GBC risk was stronger in women than in men. In contrast, Barbhuiya et al. observed in 2009 that about 67.89% of GBC patients they studied had a BMI below 18.5. The distribution of subjects in the present study, in different BMI categories given by the WHO, is presented in Table 5.

The mean height of all enrolled patients was 1.54mtrs  $\pm$  0.08 mtrs (min. 1.4 to 1.8 mtrs) with standard deviation. The average weight was 54.49kgs  $\pm$  9.51. with the lowest weight being 30kgs and highest being 84 kgs. The average BMI of patients was 23.00  $\pm$  4.13, ranging from 13.28 – 31.33. For majority of patients (61.5%, (n=59) the BMI was in the normal range-I & II, 27.1% (n=26) patients were overweight and only 3.1% (n=3) were obese. It was also observed that only 8.3% (n=8) patients were

malnourished. Overall, one-third of the patients were overweight or obese suggesting that higher BMI may increase risk of Gall Bladder Cancer (Table 5).

The SGA has been validated in a number of diverse patient populations, including cancer patients. (Gupta et al. 2008). Approximately two third of patients reported a weight loss of more than 10%. Two-thirds reported that their eating habits had changed due to the illness, with two-thirds of patients (n=60) 62.5% stating that their food intake had reduced (Figure 2).

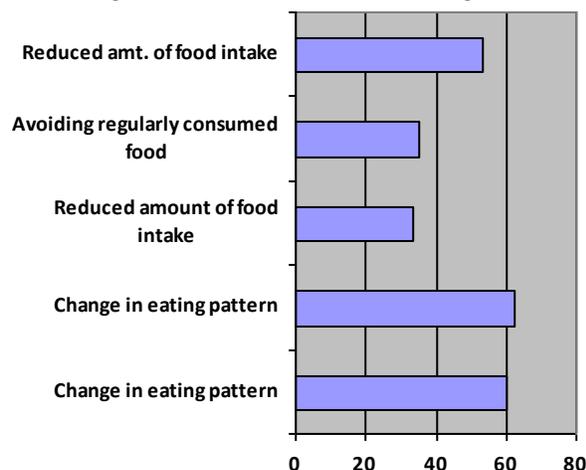


Figure 2 : Change in Dietary intake

One-third of the patients (n=32) had stopped eating certain food items which they were eating regularly. One-third of patients (n=34) showed some symptoms when they tried to eat their usual quantity of food. It was found that for 53.1% (n=51) patients the meal pattern had changed due to the cancer.

The prevalence of malnutrition may induce metabolic stress. It was found that 44.8% (n=43) patients showed no metabolic demand, but about half of the patients 54.2% (n=52) showed low to moderate metabolic demand and 1 patient had a high metabolic stress demand.

Table 6 : Symptoms observed during physical examination of patients

Category	Change	Freq	Percent
01 Muscle wasting	Normal	56	58.3
	Mild-Moderate	35	36.5
	Severe	5	5.2
	<b>Total</b>	<b>96</b>	<b>100.0</b>
02 Ankle Edema	Normal	92	95.8
	Mild-Moderate	4	4.2
	<b>Total</b>	<b>96</b>	<b>100.0</b>
03 Sacral Edema	Normal	94	97.9
	Mild-Moderate	2	2.1
	<b>Total</b>	<b>96</b>	<b>100.0</b>
04 Ascitis	Normal	91	94.8
	Mild-Moderate	5	5.2
	<b>Total</b>	<b>96</b>	<b>100.0</b>

Most of the patient BMI was in normal limits (Table 1) the physical examination correlated with the BMI findings. Approximately one-third of the patients had muscle wasting with 5% having severe muscle wasting and 4.2% had ankle edema. Ascitis was found only in 5.2% (n=5) patients. (Table 6).

The prevalence of severe malnutrition in this patient population, as determined by SGA Score – ‘C’, was 11.5% (n=11). About

half of the patients (54.2%, n=53) had an score of ‘B’ moderately malnourished, and 34.4% (n=33) patients scored ‘A’ ie. They were well nourished.

Vegetarians have fewer stones compared to non vegetarians (Dwyer, 1988). Gall stones are composed of cholesterol, bile pigments and calcium salts. A study of over 750 women showed the incidence of gall stones to be less frequent in vegetarians. One fourth of non-vegetarians compared to 12% of vegetarians had gall stones. After controlling for age and body weight, non-vegetarians were found to have a relative risk of gall stones almost twice that of the vegetarians. Vegetarians are leaner, and consume more dietary fibre and less dietary cholesterol, all of which is believed to protect against gall stone formation (Pixley, 1985).

A dietary evaluation of Gall Bladder Cancer (GBC) patients by Pandey et al. in 2002 found a significant reduction in odds ratio with the consumption of radish (OR 0.4; 95% CI 0.17-0.94), green chilli (OR 0.45; 95% CI 0.21-0.94) and sweet potato (OR 0.33; 95% CI 0.13-0.83) among vegetables, and mango (OR 0.4; 95% CI 0.16-0.99), orange (OR; 0.45; 95% CI 0.22-0.93), melon (OR 0.3; 95% CI 0.14-0.64) and papaya (OR 0.44; 95% 0.2-0.64) among fruits. A reduction in odds was seen with the consumption of cruciferous vegetables, beans, onion and turnip, and an increase in the odds with consumption of capsicum (OR 2.2), beef (OR 2.58), tea (OR 1.98), red chilli (OR 1.29) and mutton (OR 1.2), however the difference was statistically not significant. The investigators concluded that the results of the study showed a protective effect of vegetables and fruits on GB carcinogenesis, but red meat (beef and mutton) was found to be associated with increased risk of GBC. Other studies have also shown protective effect of fat and protein rich diets as well as consumption of fiber, vitamin C and vitamin E (Tominaga et al. 1979, Zatonski et al. 1992).

The data of the present study revealed that 61.5% (n=59) patients out of 96 were non vegetarians compared to only 38.5% (n=37) vegetarians. Although the findings conform with previous studies in the literature, it is difficult to conclude that non-vegetarians are at a greater risk since it is a retrospective study on a relatively small sample.

Tyagi et al. in 2009, in a population based case-control study observed that consumption of urad, moong, milk, cottage cheese and butter showed a positive relation with the risk of GBC.

The dietary intake of patients in the present study was examined (Table 7). Amounts consumed were estimated using a food frequency questionnaire.

The data revealed that the daily average cereal consumption of GBC patients was 244 gms ± 57. Average consumption of pulses was 41.6 gms ± 17 gms. The mean consumption of vegetables was very low 121g ± 59.7g and green leafy vegetable was 37gms ± 27.57. Average fruit consumption was only 5gms ± 17.32. Milk and milk product consumption was 106gms ± 42 (Table 7). It was also observed that daily average root vegetable consumption was 109 ± 45g. The mean fish consumption was 32gms ± 28. The patients consumed a moderate amount of meat and chicken, 15gms ± 24, along with sugar 15gms ± 10gms and average daily visible fat consumption was 29gms ± 10. A very low consumption of eggs (4.0 gms) and nuts (1.1gms) was recorded (Table 7)

Table 7 : Details of food items consumed

Food Items	Std		Median	Max	Min
	Mean	Dev			
Cereals	244	57	234	480	133
Dals & Pulses	41	17	42	100	0
Vegetables	121	60	120	575	33
GLV	37	28	33	100	0
Root Vegetable	109	45	117	250	0
Fruits	5	17	0	100	0
Meat & Chicken	15	24	0	67	0
Fish	32	28	0	100	0
Eggs	4	4	7	0	16
Milk /Milk Products	106	42	100	250	0
Nuts	1	5	0	33	0
Sugar	15	10	20	50	0
Oils & Fats	29	6	29	40	9

Rizwan et al. in 2010 conducted a study of 52 GBC patients where in they evaluated their dietary patterns and found that 84.62% patients were using mustard oil as a cooking medium. Similarly, in the present study, dietary history revealed that the majority 68.9% (n=67), were using mustard oil and the average visible fat intake was 29g/day (Figure 3).

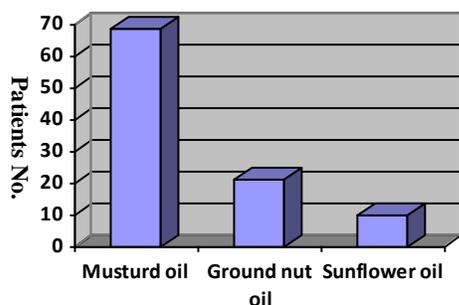


Figure 3: Type of oil used for cooking

High energy and high total carbohydrate intake have both been linked to GBC. Zatonski et al. in 1997, observed that the odds ratio associated with high energy intake was 2.0, while the ratio associated with total carbohydrate consumption was 11.3. A significant reduction in risk has been associated with increased vitamin B6 and vitamin E consumption. Vitamin C, fat, and dietary fiber intake have also been shown to provide modest protection (Zatonski et al. 1997).

In 2006, a case-control study was conducted by Rai et al. The sample consisted of 153 cases of Gall Bladder Cancer (GBC) patients and 153 controls of gallstone disease (GSD). They found that dietary Intake of almost all the nutrients was far below the recommendations of Indian Council of Medical Research.

In the present study, the average intake of most of the nutrients of GBC patients was lower than the recommendations of ICMR(2011). The results (Table No 8) showed that the mean intakes per day were as follows: energy, 1717 Kcal (SD= ± 294) and protein 49gms (SD= ± 10.5), carbohydrate 269 gms (SD= ± 50) and fat 43 gms (SD =± 8.2). Mean total dietary fibre consumption was 24 gms (SD = ±11.5) The average consumption of micro nutrients were, Iron 14gms (SD= ± 4.5) β carotene consumption was 1797 µg (SD = ± 503), folic acid 195 µg (SD = ± 51.6), vitamin -C 59mg. (SD = ± 10.5) and sodium was 141mgs (SD = ± 36.4). Table No. 08. Calcium consumption was found to be marginally above ICMR recommendations 440mg (SD = ± 141.99).

Table 8. Nutrient intake of GBC patients (3 Day Dietary recall)

Nutrients	Std		Median	Min	Max
	Avg	Dev			
Energy (Kcal)	1717	294	1677	1053	2789
Carbohydrate (gms)	269	50	266	171	413
Protein (gms)	49	10	49	24	85
Fat (gms)	43	8	42	27	92
Minerals (gms)	10	2.8	10	4	21
Crude fibre (mg)	6	2	6	2	11
Calcium (mg)	440	142	413	278	1568
Phosphorous (mg)	1120	322	1145	532	2265
Iron (mg)	14	4.5	15	5	25
Carotene (µg)	1797	503	1780	440	3568
Thiamine (mg)	1	0.47	1	0	3
Riboflavin (mg)	1	0.16	1	0	1
Niacin (mg)	12	3.7	12	5	21
Vitamin -B6 (mg)	0	0.4	0	0	3
Folic acid (µg)	195	51.6	206	68	319
Vitamin-C (mg)	59	10	60	33	83
Choline (mg)	81	33	75	20	147
Mg (mg)	716	290	682	440	3273
Sodium (mg)	141	36	139	76	404
Potassium (mg)	1675	452	1753	737	3923
Copper (mg)	2	0.6	2	1	4
Mn (mg)	6	3	5	2	20
Molebdenium (mg)	0	0.11	0	0	1
Zinc (mg)	7	1.8	6	3	11
Crude fibre (mg)	0	0.01	0	0	0
Selenium (mg)	396	117	404	91	722
Chloride (mg)	124	33	127	29	210
Oxalic acid (mg)	158	44	171	27	401
Phytin (mg)	203	54	188	124	499
Phytin P as % of total P (mg)	235	61	233	105	395
TDF (gms)	24	11	34	11	63

The following nutrients were found to be negatively associated with the White Blood Cells count. iron ( $r = -0.170$ ,  $P$  value= 0.049), folic acid ( $r = -0.184$ ,  $P$  Value=0.036), and chromium ( $r = -0.186$ ,  $P$  value = 0.035 ).

The following nutrients such as Protein ( $r = 0.186$ ,  $P$  value = 0.035), Calcium ( $r = 0.202$ ,  $P$  value =.024), Folic acid ( $r = 0.213$ ,  $P$  value =.018), Magnesium ( $r = 0.320$ ,  $P$  value =0.001), Copper ( $r = 0.259$ ,  $P$  value =0.005), Manganese ( $r = 0.237$ ,  $P$  value =0.010) and Zinc ( $r = 0.215$ ,  $P$  value =0.018) were found to be positively correlated with platelets.

## Conclusions

From the study conducted on Gall Bladder cancer (GBC) patients it can be concluded that, In this study more women than men had GBC. It showed an increase with age in both sexes. Post menopausal women had a significant risk of GBC than the menstruating women. The higher prevalence among women suggests that hormone may play a role. A population with low socio economic status and with poor education seems to promote GBC incidents.

Various non dietary habits like smoking, drinking and tobacco chewing were found to be insignificant with gallbladder cancer incidents. Occupational exposures in the rubber, automobile, wood-finishing, oil, paper, chemical, textile, shoe, fiber and metal-fabricating industries was found to be insignificant. The dietary habits revealed a high risk was associated with the less consumption of vegetables and fruits. The Nutrient intake of gall bladder patients was found to be less than the ICMR recommendations.

In North India, GBC is more prevalent than other parts of India

where, mustard oil is commonly used as a cooking medium. It may be further investigated that the cooking medium used may contain significant amount of carcinogenic compounds. Mustard oil can be proposed as a factor responsible for increased prevalence of GBC.

Medical history like Typhoid, Diabetes, Hypertension, Hysterectomy were found to be insignificant. But patients with gallstones are at a higher risk of developing GBC.

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### References

- American Cancer Society (2008) Key Statistics for Gallbladder Cancer.
- Andrew KD (1983) Gallstone Size and the Risk of Gallbladder Cancer. *JAMA*. 250 (17):2323-2326
- Barbhuiya M, Singh T, Gupta S et al (2009) Incidence of gall bladder cancer in rural and semi-urban population of north central India: A first insight. *The Internet Journal of Epidemiology*. Volume 7 Number 2
- Batra Y, Pal S, Dutta U (2005) Gallbladder cancer in India: A dismal picture, *Journal of Gastroenterology and Hepatology*. Volume 20, Issue 2, pages 309–314
- Bornstein FP (1970) Gallbladder carcinoma in the Mexican population of the southwestern United States. *Path Microbiol*, 35, 189-91
- Bushra W, Nighat K, Naila IH et al (2010) Age and Gender related frequency of cancer in chronic cholelithiasis, *Journal of Surgery Pakistan (International)* 15 (1)
- Chaurasia P, Thakur MK, and Shukla HS (1999) What Causes Cancer Gallbladder?: A Review Volume 11 (1999), Issue 4, Pages 217-224
- Dewar MR and Parfitt GJ (1954) An investigation of the physical properties of saliva and their relationship to the mucin content. *J dent Res* 33:596-605
- Dhir V and Mohandas KM (1999) Epidemiology of digestive tract cancers in India IV. Gall bladder and pancreas. *Indian J Gastroenterol*. 18: 24-28
- Diplock AT (1991) Antioxidant nutrients and disease prevention: An overview. *Am J Clin Nutr* 53:189S-93S
- Dutta U, Nagi B, Garg P et al (2005) Research papers: Gastrointestinal Cancer, *European Journal of Cancer Prevention* - Volume 14 - Issue 4 - pp 381-385
- Dwyer JT (1988) Health aspects of Vegetarian diets. *Am J Clin Nutr* 48:3:712-738
- Enriqueta B, Katy H, Marcelo E et al (2010) Gallbladder cancer: incidence and survival in a high-risk area of Chile, *Int. J. Cancer*: 127, 2446–2454 VC 2010 UICC, *J Post grad Med* 50:145-9
- Editorial-II (2008) Diet and Gallbladder Cancer. *Indian Journal Of Medical & Pediatric Oncology* Vol. 29 No 1
- Gupta D, Carolyn A, Lammersfeld et al (2008) Can subjective global assessment of nutritional status predict survival in ovarian cancer?, *Journal of ovarian research* 155: 1:5
- Hsing AW, Rashid A, Devesa SS et al (2006) Biliary tract cancer, *Cancer epidemiology and prevention*, 3rd edn. New York: Oxford University Press 787–800
- ICMR (2001) National Cancer Registry Programme: Consolidated report of the population based cancer registries 1990-1996. Incidence and distribution of cancer. New Delhi: Indian Council of Medical Research p. 52-3
- Jehad B, Jeffrey C. Dunkelberg (2006) *CANCER*, Volume 106, Number 2, 434-440
- Kato K, Akai S, Tominaga S et al (1989) A case-control study of biliary tract cancer in Nigata Prefecture, Japan: *Jpn J Cancer Res* 80:932-8
- Kratzer W, Kachele V, Mason RA et al (1997) Gallstone prevalence in relation to smoking, alcohol, coffee consumption and nutrition. The Ulm gallstone study. *Sc and J Gastroenterology* 32:953-8
- Larsson SC and Wolk A (2007) Obesity and the risk of gallbladder cancer: a meta-analysis'. *Division of Nutritional Epidemiology, The National Institute of Environmental Medicine, Karolinska Institute, Box 210, SE-17177 Stockholm, Sweden*
- Lazcano-Ponce EC, Miquel JF, Munoz N et al (2001) Epidemiology and molecular pathology of gallbladder cancer. *CA Cancer J Clin* 51: 349–364
- Leitzmann MF, Willett WC, Rimm EB et al (1999) A prospective study of coffee consumption and the risk of symptomatic gallstone disease in men. *JAMA* 281:2106–2112
- Leitzmann MF, Rimm EB, Willett WC (1999) Recreational physical activity and the risk of cholecystectomy in women. *N Engl J Med*. 341(11):777-84.
- Malhotra SL (1967) Geographical distribution of gastrointestinal cancers in India with special reference to causation. *Gut* 8:361-72
- Malin D, Ernest H, Rosenbaum et al (2002) *Everyone's Guide to Cancer Therapy*. 4th edition
- Manoj P and Vijay KS (2004) *Gall Bladder Cancer*, Jaypee Brothers Medical Publishers (P) Ltd. 1<sup>st</sup> Edition
- Moerman CJ, Bueno de Mesquita HB, Smeets FW(1995) Consumption of foods and micronutrients and the risk of cancer of the biliary tract. *Prev Med* 24:591-602
- Moerman CJ, Bueno de Mesquita HB, Runia S (1993) Dietary sugar intake in the aetiology of biliary tract cancer. *Int J Epidemiology* 22:207-14
- Murthy NS and Mathew A (2004) *Cancer Epidemiology, Prevention and control*. Current science Vol 4, 518-527
- Negri E, La Vecchia C, Franceschi S et al (1991) Vegetable and Fruit Consumption and Cancer risk. *Int J Cancer* 48:350-4
- Nitenberg G and Raynard B (2000) Nutritional support of the cancer patient: Issues and dilemmas. *Critical Rev Oncology Hematology* 34:137–168
- Pandey M, Shukla VK (2002) Diet and Gallbladder Cancer: A case control study. *Eur J Cancer Prev* 11:1-4
- Parkin DM, Whelan SL, Ferlay J et al (1997) *Cancer incidence in five continents*. Vol. VII. IARC. Sci. Publ. 143
- Pixley F, Wilson D, McPherson K et al (1985) Effect of vegetarianism on development of gallstones in women. *BMJ*. 291:11–12
- Potter JD (1997) *Food, Nutrition and the prevention of cancer: A global perspective*. Washington DC: American Institute of Cancer Research p. 198-201
- Pritchard CC, Yeh MM (2009) Pathology and diagnostic pitfalls of cholangiocarcinoma. Rising incidence of an old cancer. *Pathology Case Review* 14(1):28-33
- Rai A, Mohapatra SC and Shukla HS (2004) A review of association of dietary factors in gallbladder cancer. *Indian J Cancer* 41:147-51
- Rajagopalan V, Daines WP, Grossbard ML et al (2004) Gallbladder and biliary tract carcinoma: A

- comprehensive update, Part 1. Oncology (Huntingt) 2004, 18:889-96.
- Ramkumar J, Mallika T and Rai A (2006) An Objective Assessment of Demography of Gallbladder Cancer. *Journal of Surgical Oncology* 93:610-614
- Randi G, Franceschi S and La Vecchia C (2006) Gallbladder cancer worldwide: geographical distribution and risk factors. *Int J Cancer* 118(7):1591-602
- Renard P, Boutron MC, Faivre J et al (1987) Biliary tract cancers in Cote-d'Or (France): incidence and natural history. *J Epidemiol Community Health* ;41:344-348 doi:10.1136/jech.41.4.344
- Rizvi TJ and Zuberi SJ (2003) Risk factors for gallbladder cancer in Karachi. *J Ayub Med Coll Abbottabad* 15:16-8
- Rizwan AK, Shagufta W, Shahid S et al (2010) Advanced presentation of Gallbladder cancer: Epidemioclinicopathological study to evaluate the risk factors and assess the outcome. *J Pak Med Association* 217-219
- Roa J, Roa I and De Aretxabala X (2004) cancer de la vesícula biliar. *Rev Med Chil* 132: 955-60
- Satyanarayana L and Asthana S (2008) Life time risk for development of ten major cancers in India and its trends over the years 1982 to 2000. *Indian J Med Sci.* 62(2):35-44
- Scott TE, Carroll M, Cogliano FD et al (1999) A case-control assessment of risk factors for gallbladder carcinoma. *Dig Dis Sci* 44:1619-
- Schottenfeld D and Fraumeni J (2006) *Cancer. Epidemiology and Prevention.* 3<sup>rd</sup>. Oxford University Press 787-800
- Serra I, Yamamoto M, Calvo A et al (2002) Association of Chili pepper consumption, low socioeconomic status and longstanding gallstones with gallbladder cancer in a Chilean population. *Int J Cancer* 102:407-11
- Shukla VK, Chauhan VS, Mishra RN et al (2008) Lifestyle, reproductive factors and risk of gallbladder cancer. *Singapore Med J* 49 (11) : 912
- Singh RP, Dhanalakshmi S and Agarwal R (2002) Phytochemicals as cell cycle modulators- a less toxic approach in halting human cancers. *Cell Cyle* 1:156-61
- Steinmetz KA and Potter JD (1991) Vegetables, fruits and cancer. *Epidemiology. Cancer Causes Control* 2:325-57
- Strom BL, Soloway RD, Rios - Dalenz JL et al (1995) Risk factors for gallbladder cancer. *Cancer* 76:1747-56
- Tominaga S and Kato I (1990) Changing patterns of cancer and diet in Japan. *Recent Progress in Research on Nutrition and Cancer* Wiley- Liss, Inc 1-10
- Tyagi BB, Manoharan N and Raina V (2008) Risk Factors for Gallbladder Cancer : A Population Based Case-Control Study in Delhi. *Indian Journal Of Medical & Pediatric Oncology* , Vol. 29, No 1,16-26
- Wattenberg LW, Hanley AB, Barany G et al (1986) Inhibition of carcinogenesis by some minor dietary constituents. In: *Diet, Nutrition and Cancer.* Ed Hayashi Y, Japan, Tokyo: Japan Sci Soc Press 193-203
- Yagyu K, Kikuchi S et al (2008) Cigarette smoking, alcohol drinking and the risk of gallbladder cancer death: a prospective cohort study in Japan. *Int. J Cancer* 15;122(4):924-9
- Zatonski WA, La Vecchia C, Przewozniak K et al (1992) Risk factors for gallbladder cancer: A Polish case-control study. *Int J Cancer* 51:707-11
- Zatonski WA, Lowenfels AB, Boyle P et al (1997) Epidemiologic aspects of gallbladder cancer: A case-control study of the SEARCH Program of the International Agency for Research on Cancer. *J Natl Cancer Inst* 89:1132-8