INTERNATIONAL JOURNAL OF MEDICAL AND APPLIED SCIENCES
Earthjournals Publisher
E-ISSN:2320-3137
www.earthjournals.org

RESEARCH ARTICLE

GALL BLADDER CANCER: A RETROSPECTIVE STUDY IN A TERTIARY CARE HOSPITAL EXPERIENCE

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Abstract

Introduction - Gall bladder cancer has peculiar geographical distribution being common in central and South America in central and South America, Central and Eastern Europe, Japan and Northern India. It is also common in certain ethnic groups eg. Native America, Indian and Hispanics. It is the 5th most commonest gastrointestinal malignancy. In India gall bladder cancer incidence varies within country.

In India during 2001 the estimated number of gall bladder cancer was 14,986 and is likely to increase to 23,750 by 2016 as a result of aging and increase in size of population. Carcinoma of the gall bladder is two to six times more common in women than men. Incidence increases with age and more than 75% of patients with this malignancy are older than 65 years. Several possible etiological factors have been implicated for gall bladder cancer. Which include typhoid carrier state, dietary factors, smoking, high parity, Post menopausal, chemical carcinoma cholilitheasis.

Method – A retrospective study was carried out in Radiation oncology department, IGIMS, Patna with carcinoma of the gall bladder who were attended and treated in the department from January 2011 to December 2014. These patients' data were analysed according to their age, sex, economical status, personal habits, dietary habits, parity, literacy status.

Result – A total of 970 patients were analysed with male; female ratio was 1:3.5. Their ages ranged from 20 to 80 years. Most of the patients affected by gall bladder carcinoma were females non-vegetarian, smokers, illiterate, multipara and low socio-economical status group. In India most affected age group was 6th decade and in females 5th decade.

Conclusion – Our study concludes that post menopausal, illiterate females with lower socio economic status, non vegetarian, multiparity were more affected. Generally patients ignored their problems for quite longer duration due to illiteracy, poor financial status later on presented with advance stage of disease with poor outcome.

Keywords: Gall Bladder Cancer**,** retrospective study

INTRODUCTION

Gall bladder cancer was first described by Destoll in 1777[1]. Gall bladder cancer is a relatively uncommon cancer. It has peculiar geographical distribution being common in central and South America, central and Eastern Europe, Japan and Northern India. It is also common in certain ethnic groups eg. native America Indians and Hispanics[2]. It is fifth commonest gastrointestinal malignancy (following colon, pancreas, stomach and oesophagus) and the most common biliary tract malignancy in the USA. It is rare in Western world including the USA, UK, Canada, Australia and New Zealand where the incidence rates ranges between 0.4 and 0.8 in men and between 0.6 and 1.4 in women per 100,000 populations. However high incidence rates upto 2-4

in men and upto 4-6 in women have been reported from the various countries in central and South America, Central and Eastern Europe including Japan. In Chile gall bladder cancer is the leading cause of death from cancer among women[3].

Various epidemiological reviews have reported that gall bladder cancer is rare in India [4,5,6]. These observations are based on incidence rates of 0.5 and 1.3 per 100,000 populations in men and women respectively, reported from Mumbai in Western India. However the incidence of gall bladder cancer varies widely within India. Gall bladder cancer is much more common especially in women in North and Central India than in the West and South[7].

Table 1 - Various Studies of GBC Patients Reported from India

Study	Place	Zone	Period	No. of patients
Prakash et al.	New Delhi	North	1959-73	100
Gupta et al.	Varanasi	North	1967-76	328
Talwar et al.	Chandigarh	North	not mentioned	209
Shukla et al.	Varanasi	North	1963-79	315
Chattopadhyay et al.	New Delhi	North	5 years	143
Pal et al.	Patna	North	2011-2014	970
Zargar et al.	Kashmir	North	3 years	98
Kapoor et al.	Lucknow	North	1989-94	297
Chaudhary et al.	New Delhi	North	1987-96	196
Present Study	Patna	North	2011-2014	970

In India during 2001, the estimated number of gall bladder cancer was 14.986 and is likely to increase to 23,750 by 2016 as a result of aging and increase in size of the population [8].

Carcinoma of the gall bladder is the common malignancy of the biliary tract and the third most common gastrointestinal malignancy in and around the Varanasi region of India [9].

Gall bladder carcinoma is two to six times more common in women than men, Incidence increases with age and more than 75% of patients with this malignancy are older than 65 years. Gall bladder is more common in Caucasians than in blacks and there some evidence that the incidence is increasing in younger individual [10].

The disease is encountered mainly in the sixth and seventh decades of life [11]. The overall prognosis has remained dismal with a 5 year survival of 5-10% due to late detection of the disease [12,13,14,15].

Several possible etiological factors have been implicated for gall bladder cancer, which includes chronic infection of the biliary tract (cholelithiasis) typhoid carrier state, dietary factors, genetic predisposition, chemical carcinoma, cigarette smoking, high parity post menopausal state and obesity [16,17].

Cholelithiasis is frequently associated with carcinoma gall bladder in upto 40%-100% patients and it is most common associated factor independent of age as sex [18]. The risk of carcinoma gall bladder patients with gall stones may be increased 4 to 7 times and patients with gall stones 73 cm in diameter have a much higher risk [19].

MATERIAL AND METHOD –

This is a retrospective study (Jan 2011 to Dec 2014) carried out at radiation oncology department IGIMS, Patna. The institute serves as a tertiary care centre and referral institute for Bihar and Nepal. The entire patient were histologically proven cases of carcinoma gall bladder. A total of 970 cases were analysed. All the clinical relevant details of patients where studied and analysed.

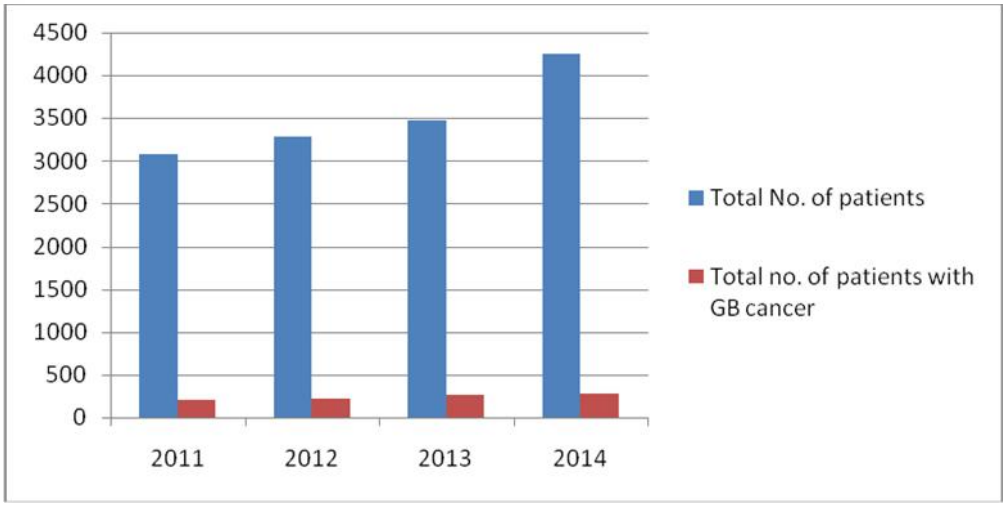
RESULTS -

During this 4 year period from 2001 to 2014, 970 patients were attended the Radiation oncology department. Overall incidence rate was 6.8% (970/14098). Table no. 2.

Table – 2

Total No. of patients of gall bladder

Year	Total no. of patients	Total no. of patients with GB Cancer	Females	Males
2011	3082	208	153 (73.5%)	55 (26.4%)
2012	3288	222	175 (78%)	47 (21%)
2013	3470	257	199 (77.4%)	58 (22.5%)
2014	4258	283	229 (80.9%)	54 (19%)
Total	14044	970 (6.9%)	756 (77.9%)	214 (22%)

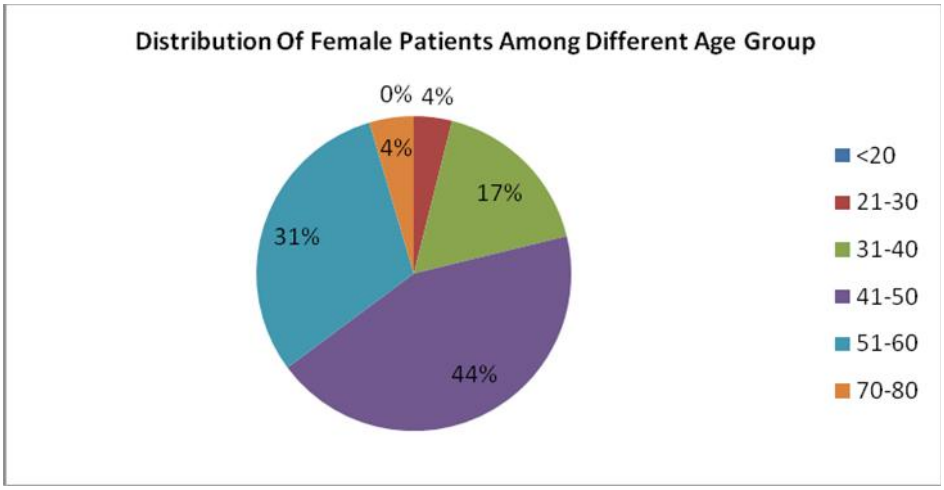


Gall bladder carcinoma was 3rd common cause of cancer among females, 1st common cause is cervix followed by Breast. The age of the patient ranged from 20-77 years of age. Table no. 3

Table – 3

Age distribution

Age	Females	Males
<20		1
21 – 30	24	7
31 – 40	106	29
41 – 50	268	54
51 – 60	188	78
61 – 70	142	44
70 – 80	28	1
Total	756	214

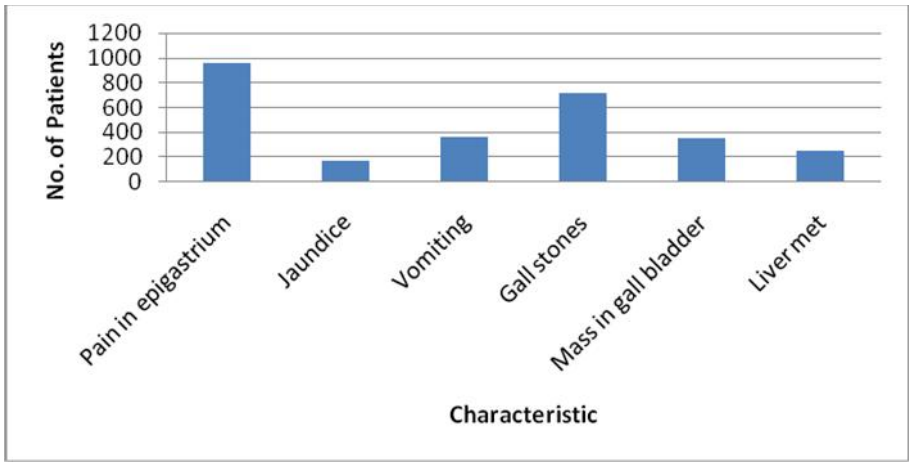


Youngest patient was 20 years of age, Muslim: oldest patients were 77 year old male. Peak age of presentation of gall bladder carcinoma was 5th decade. Male: female ratio in our analysis was 1:3.5. Most common presentation was pain in epigastrium, cholelithiasis. Majority of the patients were rural, illiterate, female multipara, low socio-economic status, non vegetarian. (Table no. 4, 5, 6,7,8,9).

Table – 4

Presentation

Characteristic	No. of patients (N=970)
Pain in epigastria	982 (92%)
Jaundice	174 (18%)
Vomiting	368 (38%)
Gall stones	717 (74%)
Mass in gall bladder	349 (36%)
Liver met	252 (26%)



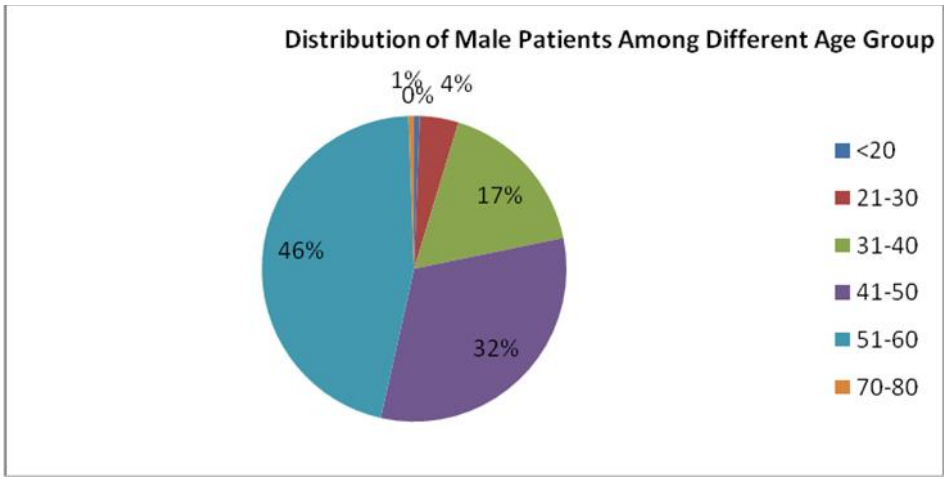


Table – 5

	No. of patients
Smoker	764 (77%)
Non Smoker	206 (23%)
Rural	770 (79.5%)
Urban	200 (20.5%)

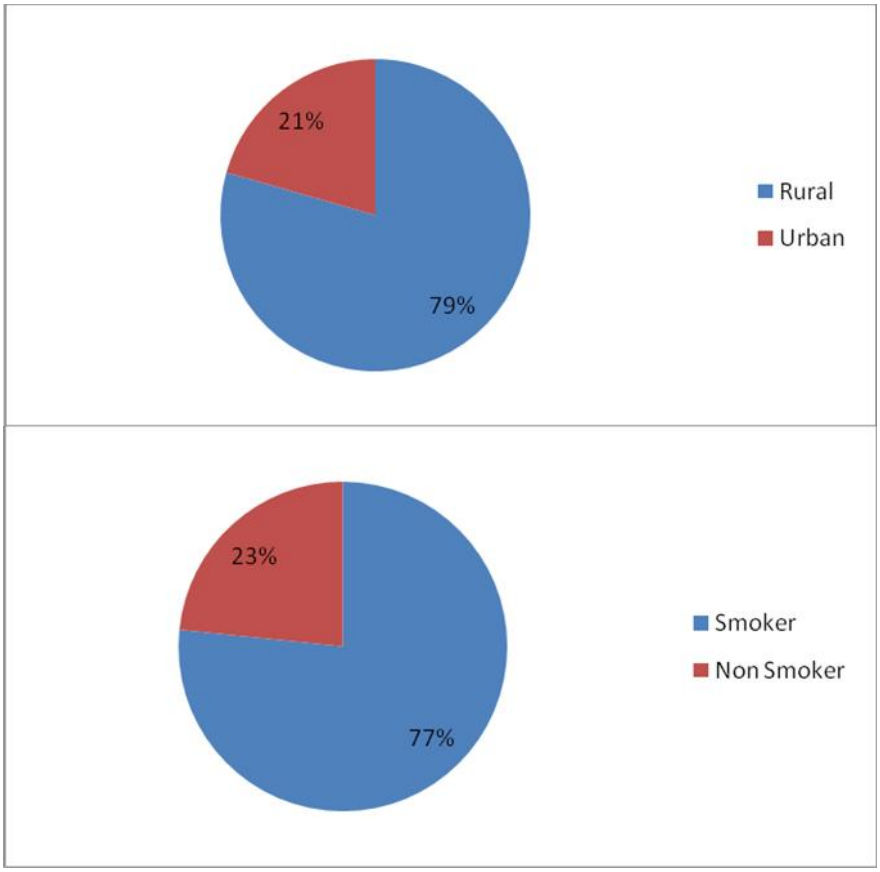


Table – 6

Literacy Status

Qualification	Females	Males
Illiterate	243 (32.6%)	22 (10%)
Upto 5th class	393 (52%)	69 (32%)
Upto 8th class	98 (13%)	72 (34%)
> 8th class	22 (3%)	51 (24%)
Total	756	214

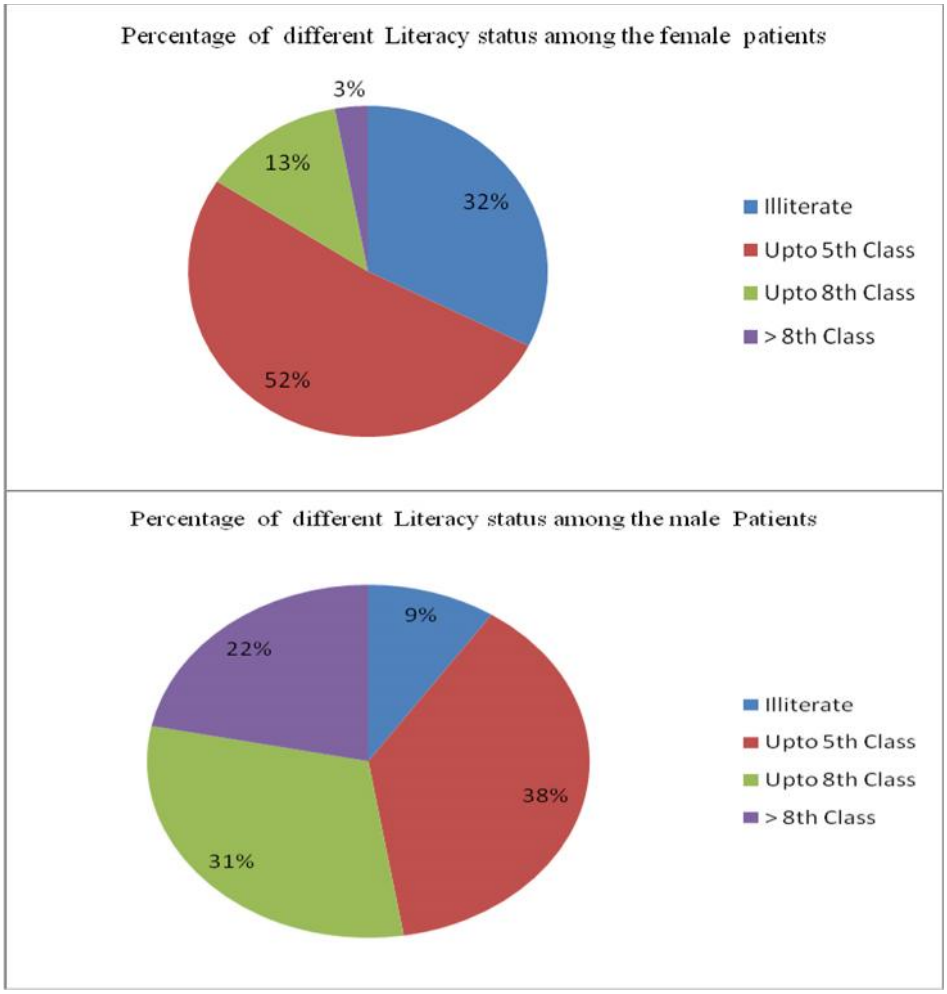


Table – 7

Dietary Pattern

Characteristic	No. of patients (N=970)
Vegetarian	223 (23%)
Non vegetarian	184 (19%)
Vegetarian and Non vegetarian	563 (58%)
Mustard oil user	436 (45%)
Mustard and Refined Oil	426 (44%)
Refined Oil	108 (11%)

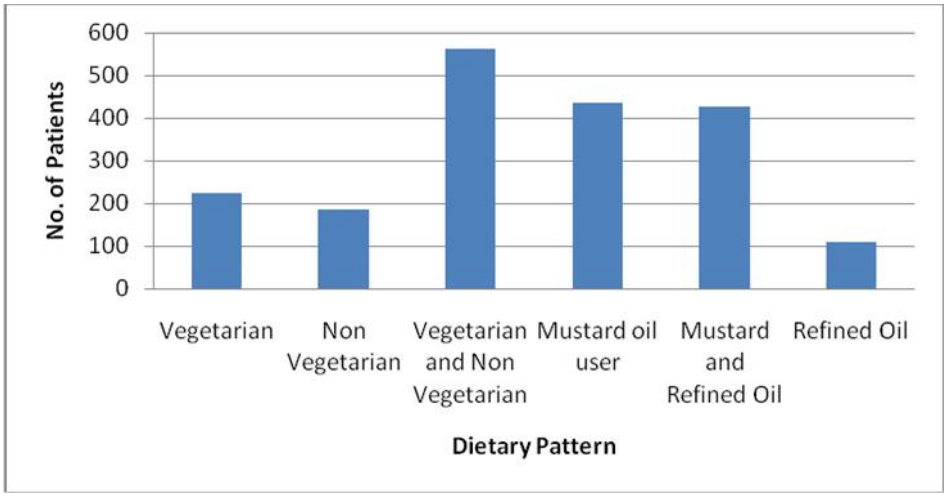


Table – 8

Socioeconomic status

Income	No. of patients
<3000 per month	117 (12%)
3-5000 per month	533 (55%)
5-10000 per month	233 (24%)
> 10000 per month	87 (9%)

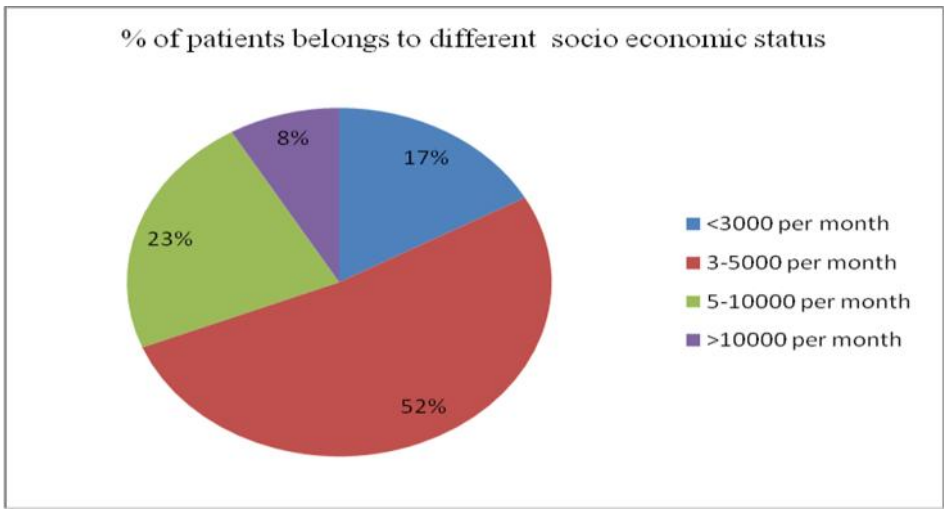


Table – 9

Parity	No. of patients
< 2	38 (5%)
2 – 4	214 (28%)
4 – 8	391 (51.7%)
> 8	113 (15%)

In our study, the age group of the patients was 20-80 years with a maximum incidence in the 5th decade of life in females and 6th decade in males.
The reported female to male ratio worldwide is 4:1 and we found 3.5:1 in our study. The incidence of gall bladder of gall bladder carcinoma was found to be more in females than in males because the incidence of gall stones and bladder diseases was common infections.

DISCUSSION -
In present analysis we have analysed the distribution of gall bladder patients according to their age, sex, socioeconomic status literacy and dietary habit, personal history and their association with the disease. Most common age group was found 5th decade in females and 6th decade in male patients. Most cases were post menopausal mustard oil user illiterate lower middle economic group. The reason might be lack of knowledge, illiteracy and other metabolic life style factors including dietary habits such as use of adulterated mustard oil, infection. Use of drinking water which may high in minerals or use of river water without filtration also contributes the disease. The greater incidence of asymptomatic gall bladder stone which were ignored by patients for the years. That can also lead to gall bladder cancer. The gall bladder stones ignored by most of the patient due to their asymptomatic nature, illiteracy, ignorance about the disease and their complications..
Our results showed that the patients who were on non vegetarian diet (more than 3 times a week), smokers were more than the vegetarian diet and non smokers. These results were supported by the study conducted by pandey et al who had shown the protective effect of vegetables on gall bladder cancer.
Increased incidence of gall bladder cancer in mustard oil users. The adulteration and carcinogenic impurities of mustard oil may be responsible for these carcinogenic changes. This study is supported by [9] who showed the elevated incidence in mustard oil users. In North India the use of mustard oil loaded with carcinoma impurities has been suggested as an etiological factor [20]. The study conducted by Sayeed Nisha [21] for incidence of gall bladder diseases in rural gangetic basin suggested that the factors appeared in this gangetic basin area was food and water. The consumption of food item chickpeas and unprotected drinking water from well, pond and river were the local factors. The proximity of river water and underground water which was high in nickel, cadmium, chromium may contribute the elevated incidence of disease.

In Delhi, Gall bladder cancer (incidence rate 6.6) was the most common cancer (following cervix, breast and ovary, incidence rates being 30.1, 28.3 and 8.7 respectively) and the most common gastrointestinal cancer in women (commoner than oesophagus 4.6, stomach 2.4 and colon 2.0) [22]. Similarly in Bhopal, Gall bladder cancer (incidence 5.2) was the fifth most common cancer in women (following cervix, breast, mouth and ovary, the incidence rates being 24.3, 21.9,6.8 and 6.2 per 100,000 population respectively and the commonest gastrointestinal cancer in women (as common as oesophagus 5.2, and commoner than colon 2.1 and stomach 1.1). In Jammu in North India gall bladder cancer was the third most common cancer (after cervix and breast) in women [23].

Recently, the Indian council of Medical Research has reported that incidence rates for gall bladder cancer in women in Northern India more than 9 per 100,000 per year are one of the highest in the world [24].

If it is diagnosed early enough it can be cured by removing the gall bladder, part of the liver and associated lymph ratio most often it is found after symptoms such as abdominal Pain. Jaundice and vomiting occur and it has spread of other organs such as the liver. The Incidence of gall bladder cancer is increasing in china [25] as well as north central India [26].

Obesity increases the risk of gall bladder cancer. Chronic cholecystitis and cholelithiasis chronic typhoid infection of gall bladder. Chronic salmonella typhi carriers have 8 to 200 times higher risk of gall bladder cancer than non carriers and 1-6% lifetime risk of development of cancer. In addition to S. typhi certain types of Helicobacter (H. Bilisand H hepaticks) and Escherichia coli have also been implicated in carcinogenesis[27 (i & ii)]

Both gall stones and gall bladder cancer predominate in females and are associated with obesity and multiple pregnancies conditions related to higher levels of estrogens suggesting that endogenous estrogens are involved in the pathogenesis of these conditions by altering bile acid composition and gall bladder motility [28,29,30]. During Pregnancy biliary sludge consisting of cholesterol crystal, Calcium bilirubinate and mucin develops in upto 30% [31], while gall stones form in 1-3% [32]. The link may be biliary sludge, a potential precursor to cholesterol gall stone formation.

In Northern India, the use of mustard oil loaded with carcinogenic impurities has been suggested [20]. High concentration of free radical oxidation products and secondary bile acids has been reported in patients with gall bladder carcinoma compared to a control group of patients with cholelithiasis [33].

A detailed geographic tracking of 773 GBC patients coming to Tata Memorial Hospital, Mumbai India, a tertiary referral centre, over six years (1990-1995) showed maximum were from Uttar Pradesh (41.9%), Bihar (35.8%), West Bengal (8.1%) and parts of Madhya Pradesh (7.3%) and Assam (7.0%). There appears to be a higher incidence of GBC in the Gangetic basin, Uttar Pradesh (65%) and Bihar 51%[34, 35]

Mustard oil from Brassica Nigra Beeds is the preferred edible oil in northern and eastern part of India specially the gangetic basin [36]. Mustard oil is often adulterated with argemone seed oil. It has been observed that the incidence of hepatic biliary/ gall bladder cancers is statistically more in the states of the gangetic basin than in other states of India [37].

CONCLUSION –

Based on these findings our study showed the females are more affected and most common age group is 5th decade. Post menopausal females illiterate, lower socio economic status group, non-vegetarian diet status were more affected. The consumption of mustard oil and use of unfiltered drinking water may also be a risk factor. Illiteracy and ignorance about their health, patients ignored their symptoms. Due to their weaker financial situation they are forced to ignore their symptoms. Patients do not want to go to the higher center or do not consult to specialist for their health problem. Generally they present with advance stage of disease. 11% of the patients presented in our analysis with obstructive symptoms like jaundice, itching, raised liver enzymes. High bilirubin level and did to turn up for their further treatment and sometimes no treatment was advisable due to high bile level and deranged liver function test.

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