## INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# EVALUATION OF RISK FACTORS ASSOCIATED WITH CARCINOMA GALLBLADDER AND OUTCOME OF TREATMENT IN RURAL AREA



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## **KEYWORDS**

#### INTRODUCTION

Gallbladder carcinoma (GBC) is the most common biliary tract cancer, accounting for 3% of all tumors [1]. GBC is hard to detect and diagnose in its early stages because it usually has very slight symptoms or is asymptomatic. But once the diagnosis is conformed, most of these patients often have metastasis and invasion. Furthermore, GBC is not sensitive to

radiotherapy and chemotherapy. All of these characteristics make GBC a highly lethal tumor with a 5-year survival rate of less than 5% [2]. Considering that survival after simple

cholecystectomy for T1 disease is reported to be near 100% [3]. It becomes increasingly necessary for early diagnosis and identifying patients at high-risk of carcinoma and offer them

prophylactic cholecystectomy. The prevalence of gallbladder cancer (GBC) shows great geographical variation. It is rare in the Western world, including the USA, UK, Canada, Australia, and New Zealand, where the incidence rates range between 0.4 and 0.8 in men and between 0.6 and 1.4 in women per 100 000 population. However, high incidence rates, up to 2-4 in men and up to 4-6 in women, have been reported from various countries in central and south America, central and eastern Europe, and Japan. Though the overall age-adjusted incidence rates of GBC in India are low (1.0 for men and 2.3 for women per 100 000 population), the incidence in women in Delhi in north India and Bhopal in central India is as high as 6.6 and 5.2, respectively, much higher than 0.6 in Chennai, and 0.8 in Bangalore in south India. In Delhi, GBC (incidence rate 6.6) was the fourth most common cancer (following cervix, breast, and ovary; incidence rates being 30.1, 28.3, and 8.7, resp.) and the most common gastrointestinal cancer in women (commoner than oesophagus 4.6, stomach 2.4, and colon 2.0) [4]. Risk factors for this neoplasm include gallstones and a history of chronic cholecystitis and an estimated 22% of patients with porcelain gallbladder will develop carcinoma. Others risk factors include choledochal cysts, anomalous pancreaticobiliary duct junctions, and gallbladder polyps > 1 cm in size. Gallbladder carcinoma has a peak incidence in the sixth and seventh decades of life and is three to five timesmore predominant in females. Primary carcinoma of the gallbladder is the most common biliary tract tumor and the sixth most common cancer affecting the gastrointestinal tract [5,6]. The majority of cases are diagnosed in the advanced stages, leading to extremely poor prognosis. The prognosis is mainly dependent on histological subtype, grade, and stage of the tumor at the time of presentation. The overall mean survival rate for patients with gallbladder cancer (GBC) is 6 months, with a 5-year survival rate of 5% [5]. GBC has a female predilection, especially women 65 years of age [7]. The commonest association of GBC is with gallstones, i.e. larger stones contributing to increased risk [8,9]. The other risk factors for developing GBC include chronic infection of the biliary tract, in particular due to Salmonella typhi, chemical exposure, cigarette smoking, high parity, post menopausal state, diet, and obesity [7,10-12]. A unique feature of GBC is that it exhibits marked geographic and ethnic variation [10-15].

## AIMS AND OBJECTIVES

- To study the etiology of carcinoma gall bladder.
- To study the clinical profile (clinical presentation as abdominal

- lump, distension, yellowish discoloration of eyes and urine) of patients presenting with carcinoma gall bladder.
- To study the pathology (type of gall bladder carcinomaadenocarcinoma or other types; well or poorly differentiated) of patients presenting with carcinoma gall bladder.

## MATERIALS AND METHODS

- The study will be conducted In Government medical college Kannauj .Department of Surgery with the help of departments of Pathology, Community Medicine and Radiodiagnosis.
- Cases: Patients included in the study will be those who present to Surgery OPD or are admitted in the Department of Surgery in GMC Kannauj with a provisional diagnosis of gall bladder carcinoma. (N=108)
- Diagnosis: Based on a combination of clinical, radiologic and histological evidence.
- Imaging studies include USG and CECT of the abdomen. For histology, either a fine needle aspiration cytology or histopathology of the resected specimen is to be done if patient undergoes surgery.

## STUDY DESIGN: CROSS-SECTIONAL TYPE OF OBSERVATIONAL STUDY.

## Inclusion criteria:

- Patients with a provisional diagnosis of gall bladder carcinoma
- Patients who give consent to take part in the study and
- Patients who give reliable answers to the questions will be included in the study.

## **Exclusion criteria:**

- Refusal to participate in the study
- Patients not able to give reliable answers
- Patients with co-morbid illnesses.
- Patients with other concomitant malignancy

Lack of radiologic or histological evidence of carcinoma gall bladder

## DIAGNOSTIC WORK-UP OF STUDY PARTICIPANTS

All the patients will go for a detailed clinical evaluation and diagnostic work-up. Their age, sex, residence, occupation, past history, family and dietary history, physical examination findings will be duly recorded. In the diagnostic work-up, haematological and biochemical parameters will be measured. Imaging studies include ultrasonography or contrast enhanced computed tomography of the whole abdomen. The patients will be managed appropriately as per the standard protocol.

## **PHYSICAL EXAMINATION**

- General examination: Nutritional status Pulse Blood pressure Pallor Icterus Lymphadenopathy Edema Systemic examination: Abdominal lump (gall bladder)
- Ascites
- · Hepatomegaly

## RADIOLOGY (USG/CECT-W/A)

- Site (most common is fundus>body>neck)
- Size
- · Liver involvement
- Nodal status
- Involvement of CBD (predicts survival), CHD, PV, HA, IHBRD
- · Omental involvement
- Involvement of other extrahepatic organs like colon and duodenum
- · Ascites
- Associated gall stones-single or multiple, size
- Associated gall bladder polyp, calcification, porcelain gall bladder

#### Histopathology

- USG guided FNAC in advanced cases
- Biopsy of resected specimen in patients undergoing surgery
- Pathological type of carcinoma and differentiation.

## **OBSERVATIONS**

Present study was conducted from July 2017 to June 2019 in the Department of Surgery , Government Medical college Kannauj on 108 patients.

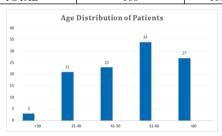
Table-1 RESIDENCE

| DISTRICT     | NUMBER OF<br>CASES | PERCENTAGE |
|--------------|--------------------|------------|
| Kannauj      | 24                 | 22.2%      |
| Kanpur Dehat | 65                 | 60.2%      |
| Auraiya      | 16                 | 14.8%      |
| Others       | 3                  | 2.8%       |
| Total        | 108                | 100%       |

The cases were residents of Kannauj and surrounding districts namely Kanpur Dehat, Auraiya, Farrukhabad and Etawah. Maximum number of cases were from Kanpur Dehat (65) followed by Kannauj (24).

Table - 2 AGE DISTRIBUTION OF PATIENTS

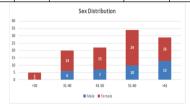
| AGE GROUP (YEARS) | NUMBER OF CASES | PERCENTAGE |
|-------------------|-----------------|------------|
| <30               | 3               | 2.8%       |
| 31-40             | 21              | 19.4%      |
| 41-50             | 23              | 21.3%      |
| 51-60             | 34              | 31.5%      |
| >60               | 27              | 25%        |
| TOTAL             | 108             | 100%       |



In our study of 108 cases, 34 cases were in the sixth decade (51-60 years). The second largest group was from seventh (61-70 years) decade.

Table - 3 SEX DISTRIBUTION

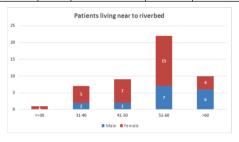
| AGE       | MALE | PERCENTAGE | FEMALE | PERCENTAGE |
|-----------|------|------------|--------|------------|
| GROUP(YR) |      |            |        |            |
| <30       | 0    | 0          | 5      | 4.6%       |
| 31-40     | 6    | 5.6%       | 14     | 13%        |
| 41-50     | 7    | 6.5%       | 15     | 13.9%      |
| 51-60     | 10   | 9.3%       | 24     | 22.2%      |
| >61       | 13   | 12.0%      | 16     | 14.8%      |
| TOTAL     | 36   | 33.3%      | 72     | 66.7%      |



Female to male ratio was 2.0:1 according to the above table. 72 patients out of the total 108 were females. This shows high prevalence of gall bladder cancer in elderly females above 50 years of age.

Table-4 PATIENTS LIVING NEAR TO RIVERBED

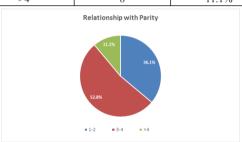
| AGE GROUP<br>(YEARS) | MALE | PERCENTAGE | FEMALE | PERCENTAGE |
|----------------------|------|------------|--------|------------|
| <=30                 | 0    | 0          | 1      | 0.9%       |
| 31-40                | 2    | 1.8%       | 5      | 4.6%       |
| 41-50                | 2    | 1.8%       | 7      | 6.5%       |
| 51-60                | 7    | 6.5%       | 15     | 13.9%      |
| >60                  | 6    | 5.6%       | 4      | 3.7%       |
| Total                | 17   | 15.7%      | 32     | 29.6%      |



Around forty-five percent patients resided near a river bed of which about fourteen percent were females in the age group 51-60 years.

Table - 5 RELATIONSHIP WITH PARITY

| NUMBER OF<br>PREGNANCY | NUMBER OF<br>CASES | PERCENTAGE OF FEMALES |
|------------------------|--------------------|-----------------------|
| 1-2                    | 26                 | 36.1%                 |
| 3-4                    | 38                 | 52.8%                 |
| >4                     | 8                  | 11.1%                 |



Of the total 72 females, 46 have parity 3 or more.

Table-6 RELATIONSHIP WITH MENSTRUAL STATE

| THE TREE TO STATE WITH THE STREET |                    |                              |  |  |
|-----------------------------------|--------------------|------------------------------|--|--|
| AGE GROUP                         | NUMBER OF<br>CASES | PERCENTAGE OF ALL<br>FEMALES |  |  |
| Premenopausal                     | 29                 | 40.3%                        |  |  |
| Postmenopausal                    | 43                 | 59.7%                        |  |  |
| Total females                     | 72                 | 100%                         |  |  |

Of total females 43 were postmenopausal, only 29 being premenopausal.



Table - 7 SOCIO-ECONOMIC STATUS

| SOCIAL STATUS | NUMBER OF<br>CASES | PERCENTAGE |
|---------------|--------------------|------------|
| Upper         | 1                  | 0.9%       |
| Upper middle  | 5                  | 4.6%       |
| Lower Middle  | 11                 | 10.2%      |
| Upper lower   | 62                 | 57.4%      |

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| Lower | 29  | 26.9% |
|-------|-----|-------|
| Total | 108 | 100%  |

The maximum number of patients belonged to the upper lower and lower class, about 84%.

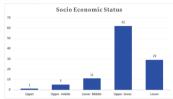
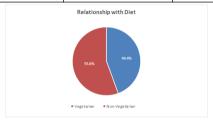


Table - 8 RELATIONSHIP WITH DIET

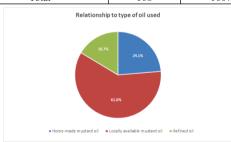
| TYPE OF DIET   | NUMBER OF CASES | PERCENTAGE |
|----------------|-----------------|------------|
| VEGETARIAN     | 48              | 44.4%      |
| NON-VEGETARIAN | 60              | 55.6%      |
| TOTAL          | 108             | 100%       |



Around fifty-six percentage of the carcinoma gall bladder patients were non-vegetarian by diet and forty-four percent were vegetarian.

Table-9 RELATIONSHIP TO TYPE OF OIL USED

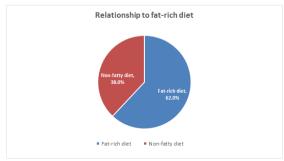
| OIL TYPE                      |       | PERCENTAGE |  |  |
|-------------------------------|-------|------------|--|--|
|                               | CASES |            |  |  |
| Home-made mustard oil         | 26    | 24.1%      |  |  |
| Locally available mustard oil | 64    | 61.0%      |  |  |
| Refined oil                   | 18    | 16.7%      |  |  |
| Total                         | 108   | 100%       |  |  |



64 out of 108 patients were consumers of locally available mustard oil and around 18 patients were consumers of refined oil.

Table - 10 RELATIONSHIPTO FAT-RICH DIET

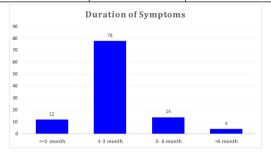
| DIET TYPE      | NUMBER OF | PERCENTAGE |
|----------------|-----------|------------|
|                | CASES     |            |
| Fat-rich diet  | 67        | 62%        |
| Non-fatty diet | 41        | 38%        |
| Total          | 108       | 100%       |



Around sixty-two percent of our patients used to take fat-rich diet and thirty-eight patients consumed non-fatty food.

Table – 11 DURATION OF SYMPTOMS

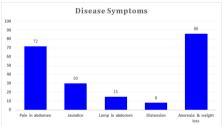
| DURATION  | NUMBER OF<br>CASES | PERCENTAGE |
|-----------|--------------------|------------|
| <=1 month | 12                 | 10%        |
| 1-3 month | 78                 | 76.25%     |
| 3-6 month | 14                 | 10%        |
| >6 month  | 4                  | 3.75%      |
| Total     | 108                | 100%       |



Maximum number of patients (76%) had disease complaints for a period between 1-3 months.

Table - 12 DISEASE SYMPTOMS

| DISEASE TYPE              | NUMBER OF CASES | PERCENTAGE |
|---------------------------|-----------------|------------|
| Pain in abdomen           | 72              | 66.7%      |
| Jaundice                  | 30              | 27.8%      |
| Lump in abdomen           | 15              | 13.9%      |
| Distension                | 8               | 7.4%       |
| Anorexia &/or weight loss | 86              | 79.6%      |
| Total                     | 108             |            |



The most common complaints were anorexia and weight loss followed by abdominal pain (66.7%).

Table – 13 EXAMINATION FINDINGS

| SIGN           | NUMBER OF CASES | PERCENTAGE |
|----------------|-----------------|------------|
| PALLOR         | 40              | 37%        |
| ICTERUS        | 39              | 36.1%      |
| ABDOMINAL LUMP | 15              | 13.9%      |
| HEPATOMEGALY   | 18              | 17.1%      |
| FREE FLUID     | 9               | 8.3%       |
| TOTAL          | 108             |            |



About 37% patients had pallor and 36% had icterus.

Table-14 RADIOLOGIC FINDINGS: SITE OF LESION

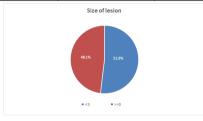
| SITE   | NUMBER OF CASES | PERCENTAGE |
|--------|-----------------|------------|
| FUNDUS | 68              | 62.9%      |
| NECK   | 22              | 20.4%      |
| BODY   | 18              | 17.1%      |
| TOTAL  | 108             | 100%       |



68 out 0f 108 patients had the site of carcinoma gall bladder as fundus, 22 patients as neck and 18 patients as body.

Table - 15 RADIOLOGIC SIZE OF LESION

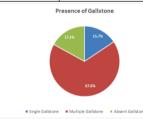
| SIZE   | NUMBER OF<br>CASES | PERCENTAGE |
|--------|--------------------|------------|
| <3 cm  | 56                 | 51.9%      |
| >=3 cm | 52                 | 48.1%      |
| Total  | 108                | 100%       |



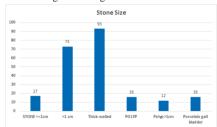
Around 52% patients had lesion size less than 3 cm.

Table - 16 PRESENCE OF GALLSTONES AND STONE SIZE

| TYPE                   | NUMBER OF<br>CASES | PERCENTAGE |  |
|------------------------|--------------------|------------|--|
| SINGLE GALLSTONE       | 17                 | 15.7%      |  |
| MULTIPLE GALLSTONE     | 73                 | 67.6%      |  |
| ABSENT GALLSTONE       | 18                 | 17.1%      |  |
| STONE <=1cm            | 17                 | 15.7%      |  |
| >1 cm                  | 73                 | 67.6%      |  |
| Thick-walled           | 93                 | 86.1%      |  |
| POLYP                  | 16                 | 14.8%      |  |
| Polyp>1cm              | 12                 | 11.1%      |  |
| Porcelain gall bladder | 16                 | 14.8%      |  |



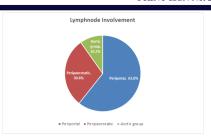
Gall stones were found radiologically in around 83% of patients. In about 68%, the stone size was more than 1 cm. Thick-walled gall bladder was a radiological finding in around 86% of cases.



Gall bladder polyp was a finding in around 14.8% cases and in 11%, it was >1 cm. Porcelain gall bladder was found in 14.8% of cases.

Table - 17 LYMPHNODE INVOLVEMENT

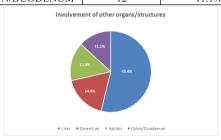
| Table - 1 / LYMPHNODE INVOLVEMENT |                    |                            |  |  |
|-----------------------------------|--------------------|----------------------------|--|--|
| LYMPHNODE                         | NUMBER OF<br>CASES | PERCENTAGE OF<br>ALL CASES |  |  |
| Periportal                        | 68                 | 63%                        |  |  |
| Peripancreatic                    | 33                 | 30.6%                      |  |  |
| Aortic group                      | 11                 | 10.2%                      |  |  |



Around 68% patients had periportal group of lymph node involvement, 30.6% had peripancreatic and 10.2% had aortic group involved.

Table - 18 INVOLVEMENT OF OTHER ORGANS/ STRUCTURES

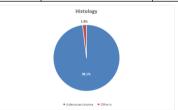
| ORGAN/STRUCTURE<br>INVOLVED | NUMBER OF<br>CASES | PERCENTAGE |
|-----------------------------|--------------------|------------|
| LIVER                       | 49                 | 45.4%      |
| OMENTUM                     | 16                 | 14.8%      |
| ASCITES                     | 14                 | 13%        |
| COLON/DUODENUM              | 12                 | 11.1%      |



Around 45.4% of patients had liver involvement and 14.8% had omental involvement. Ascites was seen in 13% and colon or duodenum involvement was seen in around 11.1% cases.

Table-19 HISTOLOGY

| TYPE           | NUMBER OF CASES | PERCENTAGE |
|----------------|-----------------|------------|
| ADENOCARCINOMA | 106             | 98.1%      |
| OTHERS         | 2               | 1.9%       |
| TOTAL          | 108             | 100%       |



In 98.1% of cases, adenocarcinoma was found in histology. In 1.9%, adenosquamous and undifferentiated tumours were seen.

Table - 20 DIFFERENTIATION

| TYPE                      | NUMBER OF CASES | PERCENTAGE |
|---------------------------|-----------------|------------|
| Well-differentiated       | 27              | 25%        |
| Moderately-differentiated | 44              | 40.7%      |
| Poorly differentiated     | 37              | 34.3%      |
| Total                     | 108             | 100%       |

Around 25% patients had a well-differentiated tumour, 40.7% had moderately-differentiated tumour and 34.3% had a poorly-differentiated tumour.

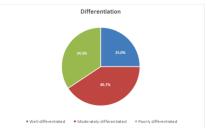
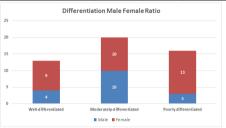


Table - 21 DIFFERENTIATION MALE FEMALE RATIO

| DIFFERENTIATION               | MALE | FEMALE | TOTAL | PERCENTAGE |
|-------------------------------|------|--------|-------|------------|
| Well-differentiated           | 4    | 9      | 13    | 26.5%      |
| Moderately-<br>differentiated | 10   | 10     | 20    | 40.8%      |
| Poorly differentiated         | 3    | 13     | 16    | 32.7%      |
| Total                         | 17   | 32     | 49    | 100%       |



Out of the total 49 patients living near the riverbed, the most common gallbladder tumour was moderately-differentiated lesion in women in females and more between the age group of 51-60 years of age.

Table – 22 MEAN AND STANDARD DEVIATION OF BIOCHEMICAL PARAMETERS

| BIOCHEMICAL PARAMETERS | MEAN    | STANDARD<br>DEVIATION |
|------------------------|---------|-----------------------|
| Haemoglobin            | 10.4694 | 1.51593               |
| TLC                    | 7305.56 | 3385.92               |
| PLATELET COUNT         | 1.80963 | 0.6126                |
| RANDOM BLOOD SUGAR     | 91.0556 | 18.1771               |
| SERUM UREA             | 50.1019 | 14.3611               |
| SERUM CREATININE       | 0.83611 | 0.26456               |
| S. TOTAL BILIRUBIN     | 4.42213 | 4.92032               |
| S. DIRECT BILIRUBIN    | 3.01481 | 3.27727               |
| S. INDIRECT BILIRUBIN  | 1.35009 | 2.56894               |
| S. PROTEIN             | 7.01759 | 7.22912               |
| S. ALBUMIN             | 3.71204 | 0.58959               |
| SGOT                   | 63.6296 | 27.6303               |
| SGPT                   | 62.4907 | 28.1815               |
| ALKALINE PHOSPHATASE   | 458.944 | 512.769               |
| S. Na+                 | 140.016 | 5.35966               |
| S. K+                  | 4.34917 | 0.63921               |
| S. Ca++                | 4.56417 | 0.57115               |

## RESULTS

## AGE INCIDENCE

The peak incidence is in 51-60 years of age. In our study of 108 cases, 34 cases were in the sixth decade (51-60 years). The second largest group was from seventh (61-70 years) decade. Mean age is 53 years.

## MALE TO FEMALE RATIO:

Out of 108 gall bladder cases, 72 were females and 36 were males. Female to male ratio in this study is 2.0:1, higher for females.

## RELATIONSHIPTO RESIDENCE NEABED

Around forty-five percent patients resided near a river bed of which about fourteen percent were females in the age group 51-60 years.

## RELATIONSHIP TO PARITY

Of the total 72 females, 46 have parity 3 or more.

## RELATIONSHIP TO MENOPAUSAL STATUS

Of total females 43 were postmenopausal, only 29 being premenopausal.

#### SOCIO-ECONOMIC STATUS

The maximum number of patients belonged to the upper lower and lower class, about 84%.

## **DIETARY FACTORS**

**TYPE OF DIET:** Around fifty-six percentage of the carcinoma gall bladder patients were non-vegetarian by diet and forty-four percent were vegetarian.

TYPE OF OIL USED: 64 out of 108 patients were consumers of

locally available mustard oil and around 18 patients were consumers of refined oil.

**FAT-RICH DIET:** Around sixty-two percent of our patients used to take fat-rich diet and thirty-eight patients consumed non-fatty food.

## **DURATION OF SYMPTOMS**

Maximum number of patients (76%) had disease complaints for a period between 1-3 months.

#### CLINICAL PRESENTATION

The most common complaints were anorexia and weight loss followed by abdominal pain (66.7%).

About 37% patients had pallor and 36% had icterus.

#### RADIOLOGICAL STUDY

SITE: 68 out 0f 108 patients had the site of carcinoma gall bladder as fundus, in 22 patients as neck and in 18 patients as body.

#### LESION SIZE:

Around 52% patients had lesion size less than 3 cm.

#### PRESENCE OF GALLSTONES:

Gall stones were found radiologically in around 83% of patients. 1n about 68%, the stone size was more than 1 cm.

Thick-walled gall bladder was a radiological finding in around 86% of cases. Gall bladder polyp was a finding in around 14.8% cases and in 11%, it was >1 cm. Porcelain gall bladder was found in 14.8% of cases. LYMPH NODAL GROUP INVOLVED: Around 68% patients had periportal group of lymph node involvement, 30.6% had peripancreatic and 10.2% had aortic group involved.

**OTHER ORGAN/STRUCTURE INVOLVEMENT:** Around 45.4% of patients had liver involvement and 14.8% had omental involvement. Ascites was seen in 13% and colon or duodenum involvement was seen in around 11.1% cases.

## HISTOPATHOLOGY

In 98.1% of cases, adenocarcinoma was found in histology. In 1.9%, adenosquamous and undifferentiated tumours were seen.

Around 25% patients had a well-differentiated tumour, 40.7% had moderately-differentiated tumour and 34.3% had a poorly-differentiated tumour.

Out of the total 49 patients living near the riverbed, the most common gallbladder tumour was moderately-differentiated lesion in females and seen more between the age group of 51-60 years of age.

## DISCUSSION

In our study, we have investigated some of the etiological, clinical and pathological characteristics of patients with carcinoma gall bladder in Kannauj and surrounding districts who presented to the indoor or outdoor facility of GMC Hospital from July 2017 to December 2018. Why these characteristics should be evaluated in relation to carcinoma gall bladder has its own considerations. Gall bladder cancer is a relatively infrequent neoplasm but shows marked geographic and socio-economic variations. It is a multi-factorial disease.

Our results show that carcinoma gall bladder is predominantly a disease of elderly females above the age of 50 years with a female to male ratio of 2:1. These results are consistent with other studies (Shukla et al.,1985,Pandey et al, 2001, Nandkumar et al.,2001) where the ratios were reported to be between 2:1 to 3:1.

The present study revealed the mean age of the patients to be 53 years, with a range of 27-80 years and sixth decade was the peak age of presentation which is comparable to results obtained from other studies from India (Shukla et al., 1985; Pandey et al., 2001; Kapoor et al., 2003) which show median age around 56 years. In contrast to this, in western countries the mean age of presentation is higher (67 years according to Beltz et al., 1974) and the peak age of incidence is in the seventh decade of life (Perpetuo et al., 1978).

The disease was found to be more common in elderly post-menopausal females and those with parity three or more as compared to pre-

menopausal females or, females with parity less than three. Andreotti et al., also showed that high parity led to an increased risk of carcinoma gall bladder in Chinese patients with biliary tract cancer. Age at menarche has been controversial; some studies have shown a late age, and others have shown an early age at menarche to be a risk factor. These observations from various studies suggest a possible role of female hormonal factors in the pathogenesis of gall bladder carcinoma. Another possibility is that there is stasis of bile during pregnancy, which may be toxic to the gall bladder mucosa.

The females residing near riverbed in North India had a higher incidence of disease as compared to males residing in the same area. The water of rivers becomes highly polluted with not only agricultural effluents but also domestic sewage and industrial wastes which are being disposed of routinely in the rivers resulting in increased concentration of pollutants like pesticides, heavy metals like chromium, lead and cadmium and industrial wastes like aromatic hydrocarbons, nitrosamines, nitrates and nitrites. Also females are more home -bound than males who are mobile and have less exposure. In our study, 69.4% of patients belonged to rural areas which included Kannauj Farrukabad, and Auraiya districts. Around 84% of our patients belong to lower and upper-lower socio-economic class according to the modified Kuppuswami SES classification. The reason behind it might be the lack of knowledge in person with lower socioeconomic status, use of locally available adulterated mustard oil, more exposure to infections and hormonal imbalance due to high parity.

The role of dietary factors in carcinoma gall bladder is now well defined. Our results showed that the disease was more common in patients who consumed non-vegetarian diet (56%), food rich in fats (62%), and in those who used locally available mustard oil (61%). This fact was supported by the study of Pandey et al, 2002 who had shown the protective effect of vegetables on gall bladder carcinogenesis while meat consumption was associated with an increased risk. The study of Misra et al, 2003 also showed that the consumption of carcinogenic impurities in mustard oil led to carcinoma gall bladder. Edible mustard oil is often adulterated with argemone oil. Sanguinarine and diethylnitrosamine are present in argemone and are known to be carcinogenic and responsible for DNA damage (Dixit et al, 2013, Ghosh et al, 2015).

Our study showed that around 76% of patients had duration of symptoms between 1-3 months and only about 14% had symptom duration more than 3 months. This shows the grave nature of carcinoma gall bladder unlike other carcinomas which have a longer duration of history due to their relatively slow growth.

The most common non-specific symptom associated was found to be anorexia and weight loss (79.6%) and most common specific symptom was pain in abdomen which was seen in around 67% of patients followed by jaundice, seen in around 28% and then lump in abdomen in 14% of patients. This is consistent with previous studies (Khan et al.,2010, Hamdani et al.,2012).

Among clinical examination, most common signs found were pallor (37%), icterus (36%) and abdominal lump was present in around 14% of patients, while ascites was clinically seen in 8% of patients.

Among radiological factors, most common site of tumour was the fundus of gall bladder (63%) then, neck (20%) and the least common was the body (17%) which has been proved in earlier studies also. The size of lesion was three centimetres or more in around 48% of cases.

Gall stones have the strongest association with carcinoma gall bladder and are present in about 65-90% of cases (Misra et al., 1995, Pandey et al.,2001, Hamdani et al.,2012). Stones >3cm confer an increased risk. Chronic trauma because of the gall stones and inflammation can induce dysplasia followed by carcinoma in situ later leading to invasive cancer. In our study, about 83% patients had radiologically evident gall stones associated with carcinoma gall bladder. In about 68% of cases, the stone size was >1cm.

Thick-walled gall bladder was a radiological finding in around 86% of cases which is a radiological pointer of gall bladder malignancy. Gall bladder polyp which is also considered a premalignant lesion was seen in 6.5% of cases and in 5.6%, it was >1cm. Porcelain gall bladder was found in 14.8% of cases. According to some studies (Stephen et al.,2001), it is associated with 12-62% of cases of carcinoma gall

bladder while recent studies show little or no association (Towfigh et al.,2001, Schnelldorfer et al.,2013).

Among lymph nodal groups, periportal involvement was seen in 63% cases, peripancreatic in 31% and aortic group in 10% cases. Liver was involved in 45% cases, omentum in 15% cases and ascites was seen in 13% of cases.

The most common histological type found was adenocarcinoma which was present in 98.1% of cases and only 1.9% had either adenosquamous or undifferentiated tumours (Beltz et al.,1974, Hamdani et al., 2012). Only 25% of all cases had well-differentiated tumours and the rest had moderately (41%) or poorly differentiated tumours (34%). Out of the total 49 patients living near the riverbed, the most common gallbladder tumour was moderately-differentiated lesion in women in females and more between the age group of 51-60 vears of age.

The information about other etiological factors like family history of gallstone, life style information, and fertility were either insufficient or incomplete for statistical analysis. Thus, here we are only presenting the percentage value of our selected parameters, but the given data might be helpful in raising a new hypothesis and in understanding of new parameters related with the development of gall bladder cancer.

#### CONCLUSION

- Gallbladder cancer is an uncommon cancer worldwide but common in North India with female predilection and advanced stage at presentation.
- Risk factors for this may include advanced age, female gender, low socio-economic status resulting in high parity, consumption of adulterated mustard oil, lack of knowledge regarding health and risk factors, chronic exposure to infections, lack of early treatment of cholelithiasis, proximity to river bed which again has a high concentration of carcinogenic pollutants being daily added to it by domestic and industrial wastes.
- Most gallbladder cancers presented as advanced stage disease and fundus was the most common site. Adenocarcinoma accounted for the majority of gallbladder cancers.
- The status of gallbladder cancer over the last century has not shown any definitive improvement in overall survival and continues to be plagued by the presence of advanced disease at diagnosis.
- This is directly related to the continued lack of sensitive screening modalities for the detection of early disease.

The future, therefore, for improved success in the management of this disease may have to be directed towards the development of sensitive and specific screening strategies with relevant improved understanding of the pathogenesis of this disease.

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