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# Observation of Incidence of Carcinoma Gallbladder in Relation To Gallstones in RIMS,Jharkhand

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***Abstract:***
***Aim :*** *To observe the incidence of carcinoma Gall-Bladder in relation to Gall-Stones in RIMS.*
***Material and method :*** *The present study comprised of 272 specimen of surgically removed gall-bladder irrespective of clinical or ultrasonological diagnosis. The diagnosis was made on the basis of detailed history, through clinical examination, ultrasonological examination and confirmed by histopathological examination.*
***Result :*** *In our study we included 276 cases in which 4 cases were inoperable and remaining 272 cases were treated with cholecystectomy. We found that 7.9%(22) of total cases had carcinoma gall bladder with stones and 0.72%(2) of carcinoma gall bladder without stone.*
***Conclusion :*** *There is very high incidence of carcinoma gall bladder (7.9%) associated with gall stones.*
***Keywords:*** *Gall bladder, carcinoma, gall stones*

## I. Introduction

The first case of carcinoma gall bladder was reported by Destoll. Gall stones have been considered as an etiogenic factor for a pretty long time. Other pathogenic conditions of the gall bladder presumably associated with the development of carcinoma are cholecystoentric fistula, Porcelain gall bladder and adenoma[1].The incidence of carcinoma gall bladder has been a subject of great controversy[2]. Incidence of gall bladder carcinoma in American population has been reported to be as high as 10 percent. Graham, 1931 has been widely cited, who reported the incidence to be 8-10 of all malignancies of women. Other American workers also report higher incidence[3].

In contrast British workers have shown much lower incidence of carcinoma gall bladder. Marshall et al [4] studied 1336 gall bladder removed surgically from 1928 to 1937 and found the incidence of carcinoma gallbladder to be 1.4%. In 1961, Marcial et al [5] studies 2813 surgically removed gall bladder found overall incidence of cancer to be 1.3%. The relationship between the presence of gall-stones and the eventual development of malignancy in the gall bladder has been widely studied by various workers. It has been postulated that gall-stones constituted an exciting factor for the production of carcinoma of gall bladder. The continual mechanical irritation of mucous membrane by an irritative substance has long been recognized as potential causes of abnormal cell proliferation. Added to this, the possible carcinogenic effect of the bile itself and the complicity of cholelithiasis in the production of gall bladder malignancy seem certain.

Accordingly to recent workers, it is the "abnormalities in bile composition" which is being blamed to be the cause of gall-stone formation, especially in case of cholesterol stones. In cholelithiasis, due to stone, other than cholesterol ones, there may be changes in the normal composition of bile due to the presence of foreign molecules. The liver secretes an excess of molecule, not ordinarily present in bile. Thus the bile becomes saturated with foreign or trace molecules, which in turn are precipitated from bile and form stones consisting of calcium bilirubinate, calcium glycocholate or calcium glycoallodioxycholate [6].

Cooke et al [2] has worked to find out the relation of carcinoma of gall bladder to different types of stones. General pattern of type of gall-stones associated with carcinoma of gall bladder did not differ from overall pattern of gall-stones found. Based on mucosal findings intestinal metaplasia is more frequent in cholesterol stones that other type of stones. The incidence of adenocarcinoma is more frequent in the cases with a stone (more often a cholesterol stone that a bilirubin stone). A retrospective study of 346 cases of removed GB which was based on histological changes and noticed a progressive increase in the average age from intestinal metaplasia to carcinoma suggesting that metaplasia carcinoma succession may occur in GB cancer[7].

There may be some relationship to the size of a stone, as it has been suggested that the risk for developing carcinoma in a patient with a 3 cm gall-stones is 10 times that for one with a stone less than 1 cm.

An unusual case of gall bladder malignancy was reported which consisted of mesenhymal sarcomatous (sarcoma) and epithelial components(adenocarcinoma)[8] .

American workers supported the idea of prophylactic cholecystectomy in cases of asymptomatic gallstones as incidence of primary gall bladder cancer in USA was more than 2.5%[9].A cinicopathological study of 100 consecutive cases of primary carcinoma of gall bladder in AIIMS suggested that early cholestectomy should be done for all cases of cholelithiasis whether symptomatic or asymptomatic provided there are no surgical contraindications[10]. Shrestha et al [11] found in their study that incidence of primary gall bladder cancer was 3.3% and concluded that every cholecystectomy specimen should be examined histopathologically to detect possible incidental carcinoma. A retrospective study done in south India found that Gall bladder cancer is uncommon in south India and its association with gallstone is low[12].

Due to increasing incidence of carcinoma gallbladder in this region ,this study has been undertaken in the tribal dominated state of Jharkhand at RIMS.

***Aims and objectives*:**

1. To observe the incidence of carcinoma gall bladder in RIMS Ranchi and its association with the gall-stones.
2. To find out relationship between carcinoma gall bladder and particular type of gall stone.

***Study area* :** The study was conducted in the Department of Surgery, RIMS,

***Study population :*** Subjects were selected from those attending surgery OPD and admitted in surgery ward in RIMS. This study was carried out from September 2012 to September 2014.This study was approved by the Ethical Committee of RIMS, Ranchi. 276 subjects were selected for the study.

## II. Methodology

The present series of work entitled "Observation of incidence of carcinoma gall bladder in relation to gall stones in RIMS" has been conducted in the Department of Surgery, RIMS, Ranchi from September 2012 to September 2014. Over 276 cases of gall bladder diseases were studied, out of which 4 cases were diagnosed as inoperable carcinoma of gall bladder which included both calculous and acalculous diseases. The materials for the study comprised of 272 specimens of surgically removed gall-bladder, irrespective of clinical or ultrasonological diagnosis. The diagnosis was made on the basis of detailed history, thorough clinical examination, ultrasonological investigation and finally confirmed by histopathological examination.

**Histological process :**

The removed gall-bladders were received in glass containers filled with formaldehyde solution and were carried to the Department of Pathology for histological examination. The processing, preparation of permanent slide and staining of tissue sample was done to begin with fixation of tissue, dehydration, clearing, paraffin impregnation section cutting, treatment of paraffin cut section, staining (Schaffer's 1953).

Routine Haematoxylin and Eosin staining was carried out. Haematoxylin was of Harriss Haematoxylin variety (10 percent Alcoholic Hamatoxylin 10 ml + 10 percent aqueous Ammonium Alum 200ml). The diagnosis was done by department of pathology.

**Statistical Analysis:** All data collected and their distribution as per age, gender and diagnosis was tabulated, and their percentage was calculated.

## III. Result

Present study consisted of clinicopathological observations in 276 cases of gall-bladder diseases out of which 272 cases were treated by cholecystectomy. The incidence of carcinoma gall-bladder in this study was 8.6% {Table-II} and maximum number of cases belonged to the age group 65 to 74 years, average age being 65 years, with male to female ratio of 1:5 {Table no-I}.The maximum duration of symptoms in patients with carcinoma ranged from 4 month to 12 years. The average maximum duration was 4.6years for females and 4 years for male patients. The average age for female case was 66 years and for male case was 58 years. Out of 24 cases of carcinoma gall-bladder, stones were found in 22cases (91%).Out of which 3 cases were inoperable. In rest 19 cases with stone, it was found that (63%) had mixed stones while cholesterol stones were found in (26%). Pigment stone was found in only (10%) {Table no-III}. Size of the stones with gall-bladder cancer ranged from 5.0mm to 3.5cm. Histological examination revealed that majority of carcinoma cases belonged to adenocarcinoma group (90%) with few cases of adenoacanthoma (10%). Clinical diagnosis of carcinoma of gall bladder was found to be difficult in 75% of cases. On the other hand histological examination of gall bladder tissue diagnosed all the cases of carcinoma of gall bladder.

## IV. Discussion

The age distribution in 24 cases of carcinoma of the gall-bladder studied in this series out of which 13 cases (54%) were between 65 to 74 years. Four cases (16.6%) belonged to the age group of 45 to 54 and 5 cases (20.8%) belonged to 55 to 64 years. Two cases (8.3%) were between 35 to 44 years of age (Table No. I). The average age incidence of carcinoma gallbladder was 65 years. When this age distribution is compared to the average age distribution of the entire series of gall-bladder diseases maximum cases were between 35 to 44 years of age and as such it is inferred that carcinoma of gall-bladder is a disease of relatively older age group.This finding is also supported by other workers[10,13,14] The youngest patient of present series was a female aged 35 years of age. In the series by Prakash et al[10] the youngest patient was a female aged 30 years. Out of total 24 cases of this series, there were 20 females and 4 males giving male female ratio of 1:5. The overall ratio of male to female with regard to gall-bladder diseases was 1:4. Thus we see that sex incidence of carcinoma cases is more or less similar to sex ratio observed in gall-bladder diseases in general. This observation of sex ratio for carcinoma cases has also been supported by other workers[10,15]. In the series of 57 patients of Chandler and Fletcher[16], 63 percent patients were women. Solan and Jackson [13] observed 57 cases of carcinoma of gallbladder where they found male to female ratio to be 1:2.6.Thus, we see that all workers are unanimous in their findings about its greater prevalence in females, more or less to the same extent as observed in this series.

There were 24 cases of carcinoma out of 276 cases accounting for 8.6 percent incidence.This incidence is slightly lower than those reported by the American Workers who reported primary carcinoma of gall-bladder to be as high as 10 percent[17]. Armanski [18] and Cleland [19] found its incidence to be 45 percent and 8 percent respectively. On the other hand, many British workers have reported a relatively lower incidence. Solan and Jackson [13] have reported that less than 1 percent carcinomas arise in gall-bladder. Gerst [15] showed 1.8 percent incidence in a series of 7496 patients with gall-bladder diseases. Holomes and Mark [14] carried out 1816 cholecystectomies and found 22 cases of carcinoma of gall-bladder (1.21 percent). It is evident from above reports that there is a curious lack of agreement as to the incidence of carcinoma gall-bladder. The incidence of present series (8.6%) also differs from many of the workers.

It is seen that out of 24 cases stones were found in 22 of them accounting for 91% when their morphological characters are considered, it was found that in operated cases with stones 63% were mixed stones, 26% were cholesterol stones and 10% were pigment stones. There are many workers who have shown close association of gallstones with carcinoma gall-bladder. Cooke et al[2] found gallstones in high proportion of patients with cancer gall-bladder. Chandler and Fletcher [16] reported that 79 percent cases are associated with gallstones in males and 83 percent cases are associated with gallstones in females. Cooke et al [2] have tried to further elaborate this association to the types of stones in his 21 cases of carcinoma gall-bladder. He found that majority (13) had mixed stones. In the present series as shown in Table No. III the most common type of stone found was mixed (63 percent) and it is more or less in accordance with observations of Cooke et a1 [2] .Cholesterol and pigment stones were also detected in the present series which again are more or less in accordance with' Cooke et al[13] .The close association of gallstones and carcinoma gall-bladder has been mentioned in literature but the exact role of gallstones in the development of carcinoma is yet to be established. However, larger size of stone and longer duration of symptoms may be attributed to carcinoma gall-bladder.

## V. Conclusion

The incidence of carcinoma gall bladder in RIMS was 8.6%. 91% of cases of carcinoma gall bladder were associated with gall stones. carcinoma of gall bladder was found in elderly patients mostly in females. carcinoma of gall bladder is mostly associated with mixed stones (63%) and less commonly with cholesterol stones (20%) and pigment stones (10%).

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**Table** – I Age Distribution Cases Of Carcinoma Gall Bladder (N=24)

| **Age group (years)** | **Patients** | | **Male** | **Female** |
|---|---|---|---|---|
| | **No.** | **%** | | |
| 25–34 | 0 | - | 0 | 0 |
| 35–44 | 2 | 8.3 | 0 | 2 |
| 45–54 | 4 | 16.6 | 1 | 3 |
| 55–64 | 5 | 20.8 | 1 | 4 |
| 65–74 | 13 | 54 | 2 | 11 |
| > 75 | 0 | - | 0 | 0 |

**Table – Ii** Incidence Of Carcinoma Gall Bladder

| **Total number of cases** | **Carcinoma gall bladder** | **Percentage** |
|---|---|---|
| 276 | 24 | 8.6 |

**Table – Iii** Associated Gall Stones In Carcinoma Gall Bladder Cases (Operated)

| **Total No. of operated cancer cases** | **Total No. of cases with stones** | **Stones** | | | | | |
|---|---|---|---|---|---|---|---|
| | | **Mixed** | | **Cholesterol** | | **Pigment** | |
| | | **No. of cases** | **%** | **No. of cases** | **%** | **No. of cases** | **%** |
| 20 | 19 | 12 | 63.1 | 5 | 26 | 2 | 10 |

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