



IJMPR



Copyright@IJMPR

## Epidemiological Study of Gallbladder Disease: An Association Between Cholelithiasis and Cancer Gall Bladder A Case-Control Study

Dr Ashish Shrivastava<sup>1</sup>; Dr Vikash Manjhi<sup>2</sup>; Dr Jyoti shrivastava<sup>3</sup>; Dr Prashant Raj Pipariya<sup>4</sup>

<sup>1</sup>Associate Professor, Department of General Surgery, G.R. Medical College, Gwalior, MP, India

<sup>2</sup>Post Graduate Resident, Department of General Surgery G.R. Medical College, Gwalior, MP, India

<sup>3</sup>Assistant Professor, Department of Physiology, G.R. Medical College, Gwalior, MP, India

<sup>4</sup>Professor, Department of General Surgery, G.R. Medical College, Gwalior, MP, India

### ABSTRACT

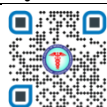
**Introduction:** Gallbladder carcinoma is a subtype of gallbladder cancer that particularly refers to primary epithelial malignancies that arise from the gallbladder. Of these, adenocarcinomas make up the vast majority (90%), while squamous cell carcinomas make up the remaining 10%. Most of the time, they only manifest symptoms when they are in advanced stages and are more common in elderly women [1]. Gallbladder cancer incidence varies widely according to region, ethnicity, and cultural differences, which points to the importance of genetic and environmental variables in the onset and spread of the disease[2]. Gallstones and chronic cholecystitis are the most frequent risk factors for the development of gallbladder cancer.

**Material and Methods:** A Case-Control Study" is to be conducted on patients admitted in various Departments of J.A. Group of Hospitals & G.R. Medical College, Gwalior, from 01 Jan. 2021 to 01 Aug. 2022. 75 patients will be selected as cases and 75 patients as controls for conducting this study.

**Result:** Females are most commonly affected with gallbladder cancer than males. Patients in the age group of 45-59 years have the highest risk of gall bladder cancer. Patients having gallstone disease were more prone to gallbladder cancer. The size of the stone also has a significant risk factor for gallbladder cancer. No. of stone also has a significant role in developing gallbladder cancer. Mustard oil consumption has shown an association with gallbladder cancer.

**Conclusion:** The main goal of the current study was to determine whether gallstone disease and gallbladder cancer are related. Carcinoma of the gallbladder was found to occur most frequently in the fourth and fifth decades of life with more prevalent among females (89.33%) than males in our study. Ultrasonographic evidence of gallstone disease was seen in most patients (53.33%) with gallbladder cancer. In this study, GBC was found in 65% of patients with multiple gallstones with stones more than 2 centimeters in size was more frequently linked to GBC. Mustard oil consumption was also associated with developing GBC Gallbladder wall thickening most common CT scan finding in our study. In this, study a significant association was found between GSD & GBC.

**Key Words:** Gallstones, Cholecystectomy, Gallbladder polyps, Gallbladder cancer



**\*Corresponding Author**

Dr. Prashant Raj Pipariya

Professor, Department of General Surgery, G.R. Medical College, Gwalior, MP, India

### INTRODUCTION

Gallbladder carcinoma is a subtype of gallbladder cancer that particularly refers to primary epithelial malignancies that arise from the gallbladder. Of these, adenocarcinomas make up the vast majority (90%), while squamous cell carcinomas make up the remaining 10%. Most of the time, they only manifest symptoms when they are in advanced stages and are more common in elderly women. Countries like Chile, Japan, India, center Europe Poland, Israel, and south Pakistan all have high rates of gall bladder cancer[3]. In comparison to Western populations, South America and Southeast Asia have a higher rate of gallbladder cancer[4]. In India, the northern and northeastern states have the highest rates of gall bladder cancer[5]. Females over 65 years old have the highest prevalence of the condition[6]. Women in northern India have the highest rates of gallbladder cancer and gallbladder disease[1]. Gallbladder cancer incidence varies widely according to region, ethnicity, and cultural differences, which points to the importance of genetic and environmental variables in the onset and spread of the disease[7].

Gallstones and chronic cholecystitis are the most frequent risk factors for the development of gallbladder cancer[8]. Gallstones are related to up to 95% of gallbladder carcinomas[2]. Patients with gallstones greater than 2–3 cm had the highest cancer risk[9]. The type of gallstone may also be significant, with cholesterol gallstones presenting the highest

risk[10]. Thus, gallstones, which are found in 60%–90% of GBC patients versus 20%–25% of an age-matched population, are the most significant risk factor for GBC. Both gallstone disease and gallbladder cancer are more prevalent in women than in males, with the prevalence rising with age and being more prevalent in ethnic groups. In addition, several other variables, such as age, gender, obesity, and a large proportion of women in the population, may increase the risk

## MATERIAL AND METHODS:

A Case-Control Study" is to be conducted on patients admitted in various Departments of J.A. Group of Hospitals & G.R. Medical College, Gwalior during a period from 01 Jan. 2021 to 01 Aug. 2022 .75 patients will be selected as cases and 75 patients as controls for conducting this study.

**Study Design:** A case-Control study.

**Source of Data:** Data Collected from the outpatient department and patients admitted in Departments of Surgery and Radiation Oncology, J.A. Group of Hospitals, Gwalior. Statistical Analysis Statistical analysis will be done by the Chi-Squared test and logistic regression analysis.

## RESULT

-Age: Most commonly affected age group is 45-59 years (n=37 i.e. 43.33%) followed by the age group 60-74 years (n=32 i.e. 42.67%) and p p-values<0.001

**Table 1: Distribution of patients according to age**

AGE DISTRIBUTION	CASE [N=75]		CONTROL [N=75]		P-VALUE
	N	%	N	%	
0-14	0	0.00%	0	0.00%	X=53.26 p<0.0001*
15-29	0	0.00%	12	16.00%	
30-44	6	8.00%	35	46.7%	
45-59	37	49.33%	18	24.00%	
60-74	32	42.67%	9	12.00%	
75-89	0	0.00%	1	1.33%	
Grand Total	75	100.00%	75	100.00%	
MEAN±SD	58.24±9.65		44.51±14.67		t=6.772 p<0.0001*

**Table 2: Distribution of patients according to gender**

GENDER	CASE [N=75]		CONTROL [N=75]		P-VALUE
	N	%	N	%	
Female	67	89.33%	56	74.67%	X=5.465 p=0.0194*
Male	8	10.67%	19	25.33%	
Grand Total	75	100.00%	75	100.00%	

-Gender: Gallbladder cancer was observed significantly higher among the female as compared to males. ( p=0.0194\*)

**Table 3: Distribution of patients according to gallstone**

GALL STONE	CASE [N=75]		CONTROL [N=75]		P-VALUE
	N	%	N	%	
YES	40	53.33%	0	0.00%	X=54.55 p<0.0001*
NO	35	46.67%	75	100.00%	
Grand Total	75	100.00%	75	100.00%	

-Presence of disease: Ultrasonography evidence of gallstones was found in more than half of the gallbladder cancer cases.

**Table 4: Distribution of patients according to oil consumption**

OIL CONSUMPTION	CASE [N=75]		CONTROL [N=75]		P-VALUE
	N	%	N	%	
MUSTARD	52	69.3%	47	62.7%	X=11.822 p=0.003
SOYABEAN	21	28%	24	32%	
MIXED	2	2.67%	4	5.33%	
Grand Total	75	100.00%	75	100.00%	

-Role of oil consumption: Consumption of mustard oil was significantly higher in cases than in controls.

**Table 5: Distribution of patients according to number of stones**

NO. OF STONE	CASE [N=75]		CONTROL [N=75]		P-VALUE
	N	%	N	%	
Single	14	35.00%	-	-	p=0.007
Multiple	26	65.00%	-	-	
Grand Total	40	100.00%	-	-	

-Number of calculus in gb lumen :Most of the GBC cases (65%) were found with ultrasonography evidence of multiple gallbladder stones.

**Table 6: Distribution of patients according to size stone**

Size of stone	N	%
<1 cm	4	10%
1-2 cm	10	25%
>2 cm	26	65%
Grand Total	40	100.00%

-Size of calculus in lumen : The most common size of gallbladder stones associated with gallbladder cancer was more than 2cm (65%) followed by 1-2cm (25%).

**Table 7: Distribution of patients according to CT findings in gall bladder cancer**

	N	%
Gall bladder thickening	49	65.3%
Gall bladder mass	26	34.7%

-Ct findings The most common CT finding in GBC was gallbladder wall thickening followed by gallbladder mass.

## DISCUSSION

This study was conducted in the Department of General Surgery at Gajra Raja Medical College in Gwalior. 75 patients were selected as cases and 75 patients were selected as control groups, both IPD and OPD patients were investigated and documented as cases of gallbladder carcinoma. Gall bladder cancer in India typically occur in patients in their 5th and 6th decade of life. The average age at diagnose in India is 51+ 11year in contrast to 71.2 + 12.5 years in the west, mean age is usually 50-55 years[11]. In this study, the age group 45-59 (n=37, 43.33 %, mean 52 years) was the most frequently affected in our study, followed by 60-74 (n=32, or 42.67 percent, mean age 67year), with a p-value of 0.001. In this study, most commonly affected age group by gall bladder cancer same as was in previous studies. Women are at 2-6 times higher risk for developing GBC. The ratio of females varies from 3:1 to 4.5:1 in various Indian series[11]. In this study, gall bladder cancer was observed significantly higher among the females as compared with males and the ratio is 8.3:1.7. In this study female: male ratio was almost 2 times higher than the previous study, which may be due to the higher incidence of GBC in this region. Gallbladder stone disease is present in 70 to 90% of Indian patients of gall bladder cancer and its presence, increases the vulnerability of gallbladder mucosal injury[11]. In this study more than half of the gall bladder cancer cases were found to have ultrasonography evidence of gallstone disease, indicating a strong connection between the two conditions. Association of gallstone disease and gallbladder cancer was

the slightly lower rate in our study possibly due to problems with detecting them on ultrasonography when they are entrapped within a mass. In a meta-analysis study excess risk of GBC was associated with being overweight or obese by 14% and 56%, respectively[12]. Most of the gallbladder cancer cases were associated with multiple gallstones (76%). The average no of multiple stone was 21 in gallbladder cancer versus 14 in controls[13]. In this study, multiple gallstones were detected by ultrasonography (USG) in 65% of cases of gallbladder cancer. In this study, the association of multiple gallstones and gallbladder cancer was slightly lower than the previous literature. This may be because on USG, sometimes few stones cannot be seen properly because of trapped stones in the mass. Gallstone size is strongly associated with gallbladder cancer, with the size of more than 1 cm (59%), was highly associated with gallbladder cancer[14]. In this study, most of the cases (65%) had more than 2 cm size gall stone followed by 1-2 cm size. (25%). This study found that the mean stone size associated with GBC was slightly larger than that in the previous studies. Consuming mustard oil and residing in high-risk areas were both significantly associated with an increased risk of GBC (OR = 7.16; 95% CI = 5.57-9.10), as opposed to not using it and living in a low-risk area[15]. In this study, mustard oil consumption is associated with significantly more cases than controls. Those who use mustard oil as their primary cooking oil account for 69% of cases. The finding of our study in this regard found comparable. Most of gallbladder cancer cases were not having a significant family history, and the familial risk of gallbladder cancer is contradictory[16]. In this study also a family history of gallbladder cancer was not a significantly associated factor. A mass replacing the gallbladder was the most typical CT scan finding for gallbladder cancer (63%). Asymmetric diffuse/focal thickening of the gallbladder wall came next (26%) and polypoidal mass (11%)[17]. In this study, the most common CT finding in gallbladder cancer was gallbladder thickening (65.3%) followed by gallbladder mass (34.7%) In this study, findings were contradictory to the previous studies.

## CONCLUSION

The main goal of the current study was to determine whether gallstone disease and gallbladder cancer are related. There are many literary works available, but some backed up our observations and some did not. Carcinoma of the gallbladder was found to occur most frequently in the fourth and fifth decades of life. GBC was found to be more prevalent among females (89.33%) than males in our study. Ultrasonographic evidence of gallstone disease was seen in the majority of patients (53.33%) with gallbladder cancer.

In this study, GBC was found in 65% of patients with multiple gallstones. Gall larger stones than 2 centimetre in size were more frequently linked to GBC. Mustard oil consumption was also associated with developing GBC. Family history of GBC has no significant role in development of GBC. Gallbladder wall thickening most common CT scan finding in our study.

In this study a significant association was found between GSD & GBC. The negative point of the study was the small sample size. Further studies with bigger sample size should be done to find a casual relation between GSD & GBC.

## REFERENCES

1. Nandakumar A, Gupta PC, Gangadharn P, Visweswara I. RN, Parkin DM(2005). Geographic pathology revisited: development of an atlas of cancer in India. *Int J Cancer*.
2. Sachs TE, Akintorin O, Tseng J(2018). How should gallbladder cancer be managed? *Adv Surg*;52(1):89–100.
3. Wistuba I Gazdar AF(2004). Gallbladder Cancer; Lessons from a rare tumor. *Nat Rev J Cancer*; 4:695-705.
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A(2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*; 68(6):394–424. [Published correction appears in *CA Cancer J Clin* 2020;70(4):313.
5. Murthy NS, Rajaram D, Gautham MS et al(2011). Trends in incidence of gallbladder cancer – Indian scenario. In: *Gastrointestinal cancer: Targets and therapy*;1:1-9.
6. Stintom LM, Shaffer EA(2012). Epidemiology of Gallbladder Disease: Cholelithiasis and Cancer. *Gut and Liver*; 6(2):172-187. 57
7. Andia ME, Hsing AW, Andreotti G, Ferreccio C(2008). Geographic variation of gallbladder cancer mortality and risk factors in Chile: a population-based ecologic study. *Int J Cancer*;123:1411–1416
8. Tsai TJ, Chan HH, Lai KH, Shih CA, Kao SS, Sun WC, Wang EM, Tsai WL, Lin KH, Yu HC, Chen WC, Wang HM, Tsay FW, Lin HS, Cheng JS, Hsu PI(2018). Gallbladder function predicts subsequent biliary complications in patients with common bile duct stones after endoscopic treatment? *BMC Gastroenterol*;18(1):32.
9. Miller G, Jarnagin WR(2008). Gallbladder carcinoma. *Eur J Surg Oncol*;34(3):306–312.
10. Hundal R, Shaffer EA(2014). Gallbladder cancer: epidemiology ad outcome. *Clin Epidemiol*; 6:99–109.
11. Dutta, U., Bush, N., Kalsi, D., Popli, P., & Kapoor, V. K. (2019). Epidemiology of gallbladder cancer in India. *Chinese clinical oncology*, 8(4), 33. <https://doi.org/10.21037/cco.2019.08.03>
12. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W(2015). Body Mass Index and Risk of Gallbladder Cancer: Systematic Review and Meta-Analysis of Observational Studies. *Nutrients*; 7(10):8321-34.
13. Roa I, Ibacache G, Roa J, Araya J, de Aretxabala X, Muñoz S(2006). Gallstones and gallbladder cancer-volume and weight of gallstones are associated with gallbladder cancer: a case-control study. *J Surg Oncol*; 93(8):624-8.
14. Alvi AR, Siddiqui NA, Zafar H(2011). Risk factors of gallbladder cancer in Karachi-a case-control study. *World J Surg Oncol*; 9:164. doi: 10.1186/1477-7819-9-164

15. Mhatre S, Richmond RC, Chatterjee N, Rajaraman P, Wang Z, Zhang H, Badwe R, Goel M, Patkar S, Shrikhande SV, Patil PS, Davey Smith G, Relton CL, Dikshit RP(2021). The Role of Gallstones in Gallbladder Cancer in India: A Mendelian Randomization Study. *Cancer Epidemiol Biomarkers* 64 Prev; 30(2):396-403. doi: 10.1158/1055-9965.EPI-20-0919. Epub 2020 Nov 13. PMID: 33187967; PMCID: PMC7611244.
16. Rawla P, Sunkara T, Muralidharan P, Raj JP(2018). Update in global trends and aetiology of hepatocellular carcinoma. *Contemporary Oncology/ Współczesna Onkologia*; 22(3):141-50.
17. Jindal G, Singal S, Birinder NA, Mittal A, Mittal S, Singal R(2018). Role of multidetector computed tomography (MDCT) in evaluation of gallbladder malignancy and its pathological correlation in an Indian rural center. *Maedica*;13(1):55.