International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 4, April 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.4.2025.163

Original Research

P53 Expression in Gallbladder Tissues and its Co-Relation with Tumor Progression in Gallbladder Cancer

Dr. Chandrawati[1], Dr. Santosh Kumar[2], Dr. Prashant Kumar[3]

[1]Associate Professor, Department of Pathology, Autonomous State Medical College, Fatehpur, Uttar Pradesh, India.
[2]Associate Professor, Department of General Medicine, Autonomous State Medical College, Fatehpur, Uttar Pradesh, India.
[3]Assistant Professor Department of General Surgery, Autonomous State Medical College, Fatehpur, Uttar Pradesh, India.

Corresponding Author
Dr. Santosh Kumar
Associate Professor, Department of General Medicine, Autonomous State Medical College, Fatehpur, Uttar Pradesh, India.

Received Date: 29 March 2025 Acceptance Date: 12 April 2025 Published: 19 April, 2025

ABSTRACT

Background: Gallbladder carcinoma is a highly lethal disease since it is usually diagnosed at an advanced stage. Oncogenes (P53) has been shown to be involved in the development and progression of gallbladder carcinoma. The present study has been conducted with an aim to study the expression patterns of P 53 in different gallbladder tissues to elucidate the role of this oncogene in carcinogenesis and to evaluate its relationship with tumor progression.

Methods: The study was conducted on histological sections from surgically resected 112 specimens of gallbladder tissue lesions, which included 66 cases of chronic cholecystitis, 34 cases of gallbladder carcinoma and 12 specimens of gallbladder controls as part of other surgical procedures with no pathology in the gall bladder.

Results: P53 expression was positive in 19 out of 34 cases (55.88%) while it was not expressed in any case of chronic cholecystitis (0/66 cases) and control gallbladders (0/12 cases). P53 expression in gallbladder cancer was significantly higher than in chronic cholecystitis and normal gallbladder specimen, ($P < 0.0001$). The level of expression of P53 increased significantly with the grade of the tumor ($p=0.05$). P53 expression did not correlate with depth of the tumor invasion (Tclassification) ($p=0.4079$) and tumor stage ($p=0.7775$).

Conclusion: In present study, it was observed that expression of P53 has a significant role in carcinogenesis and progression of gallbladder carcinoma.

Keywords: Gallbladder carcinoma, P53, **"T"-** depth of tumor invasion, stage of the lesion.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

INTRODUCTION

Gallbladder carcinoma is a highly lethal disease since it is usually diagnosed at an advanced stage.[1] Gallbladder carcinoma is the most common malignancy in the biliary tract, the fifth commonest cancer of the gastrointestinal tract.[2] In Eastern part of Uttar Pradesh, gallbladder carcinoma is the third most common cancer of the digestive tract. The disease is mainly seen in sixth and seventh decade of life.[3]

A combination of predisposing factors makes gall bladder carcinoma a unique tumor and offers potential for understanding cancer pathogenesis. These factors include ethnicity, genetic predisposition, geographic location, female gender, chronic inflammation, and congenital developmental abnormalities.[4] Epidemiologic studies have indicated a very strong association of this cancer with gender, ethnicity, and geographic distribution.[5] It is one of the obesity associated cancers and positively correlates with prolonged cholelithiasis (gallstone) and cholecystitis.[6]

Tumor protein p53, also known as p53, cellular tumor antigen p53, phosphoproteinp53, or tumor suppressor p53, is a tumor suppressor gene product that in humans is encoded by the TP53 gene.[7]

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

Inactivation of the p53 tumor suppressor gene is the most common genetic alteration in human cancers, and the prognostic significance of p53 over-expression has been reported in several malignancies, including those of the stomach, colon, and endometrium.[8-10] Available literature revealed that p53 protein expression is also seen in gallbladder cancer by using various techniques in various studies.[11]

Tumor suppressor genes (p53) have been shown to be involved in the development and progression of gallbladder carcinoma.[12]

P53 nuclear expression is significantly higher in gallbladder carcinoma.[12] P53 expression correlates with increasing tumor grade, thus suggesting a role for these genes in tumor progression of Gallbladder carcinoma.[12,13,14]

The present study has been conducted with an aim to study the expression patterns of p53 in different gallbladder tissues to elucidate the role of p53 in carcinogenesis and to evaluate its relationship with tumor invasion and differentiation, nodal involvement, metastasis, and stage of the lesions.

RESEARCH METHODOLOGY

In this present Cross-sectional study a total of 112 cases were taken for study during August 2023 to September 2024. The study was conducted on histological sections from surgically resected specimens of gallbladder carcinoma which included 66 cases of chronic cholecystitis, 34 cases of gallbladder carcinoma and 12 specimens of gallbladder controls from resections of gallbladder as part of other procedures with no pathology in the gall bladder.

Selection of cases

Cases were selected on the basis of their final histopathologic diagnosis and their clinicopathologic data were analyzed.

After taking informed consent, histopathological examination and immunohistochemical analysis of p53 expression on all selected gallbladder tissues was done.

Inclusion Criteria

1. Clinically suspected cases of benign as well as cancerous lesions of gallbladder were included.
2. Patients who agreed to sign on consent form.

Exclusion Criteria

1. Autolysed sample
2. Inadequate sample

Assessment of p53 staining

P53 expression was scored as percentage of the nuclei stained. P53 expression was judged positive when more than 5% cells were stained**.** In each high positive area, 1000 cells were counted and for each case five such areas were selected.

Data analysis and statistical tools for observation and result of the study

- Appropriate statistical tools were adopted to do data analysis. Analysis was done by data sorting method, classified by tabulation and presentation by pie charts, and histograms. The results were scored semiquantitatively and statistical analysis performed.
- A statistician's help was sought for interpretation of results. Statistical analysis was done using **chi square test** to determine the association between two or more than two variables, with the following formula:
- -If O_{ij} is the observed frequency and E_{ij} the expected frequency, corresponding to the i^{th} condition and the j^{th} group, then chi-square formula is:

$$\chi^2 = \sum_i \sum_j \frac{(O_{ij} - E_{ij})^2}{E_{ij}}$$

OBSERVATION AND RESULTS

Study Population

A total of 112 cases of gallbladder lesions including 66 cases of chronic cholecystitis and 34 cases of gallbladder adenocarcinoma and 12 specimens of normal gallbladder which served as controls were studied. Expression of p53 was analysed immunohistochemically.

Observations were made in terms of the relationship of p53 expression with tumor differentiation, invasion, nodal involvement, metastasis and stage of the disease.

Gallbladder tissues	Number of cases	Percentage (%)
Normal (control) gallbladder	12	10.7
Chronic cholecystitis	66	58.9
Gallbladder cancer	34	30.3
Total	112	100%

Table-1: Distribution of gallbladder lesions

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

The age of total (112) patients ranged from 21-80 years with a mean and standard deviation of 40.90 ± 12.18 in chronic cholecystitis cases and 59.12 ± 9.11 in gallbladder cancer cases.
Among chronic cholecystitis lesions, the maximum number of cases, i.e., 23 out of 66 cases (34.84%) were found in age group of 41-50 years followed by 18 cases (27.27%) in 51-60 years age group.
Out of 66 benign lesions, the total number of female cases were 53(80.30%) and 13 cases (19.69%) were male with F:M ratio of 4:1 and out of 34 malignant lesions the total number of female cases were 28 (82.35%)and 06 cases (17.64%) were male with F:M ratio of 4.6:1 hence showing the female preponderance in both types of lesions.
In gallbladder cancer cases, maximum number of 15 out of 34 cases(44.11%) were in the age group of 51-60 years, followed by 26.47% in 61-70 years age group.

	No. of cases	**Percentage (%)**
Chronic cholecystitis	60	90.90
Chronic cholecystitis with hyperplasia	04	6.06
Chronic cholecystitis with metaplasia	02	3.03
TOTAL	66	100%

Table-2: Distribution of chronic cholecystitis cases according to histopathological finding

Histological Type	**No. of cases**	**Percentage (%)**
Well differentiated adenocarcinoma	09	26.47
Moderately differentiated adenocarcinoma	20	58.82
Poorly differentiated adenocarcinoma	05	14.70
TOTAL	34	100

Table- 3: Distribution of gallbladder adenocarcinoma cases on the basis of histological (tumor) grade

Gallbladder tissues	**Gallbladder cancer(n=34) (%)**	**Cholecystitis (n=66) (%)**	**Control gallbladder (n=12) (%)**	**P value**
P53 expression	19/34 (55.88%)	0/66 (0%)	0/12 (0%)	0.0001

Table-4: Comparative evaluation of p53 expression in different gallbladder tissues

In gallbladder cancer, P53 expression was positive in 19 out of 34 cases (55.88%). Expression was not observed in chronic cholecystitis (0 of 66) and in control gallbladders (0 of 12). On statistical analysis, p53 expression in gallbladder cancer was significantly higher than in chronic cholecystitis and normal gallbladder specimen, ($P < 0.0001$). (Table-4)

Tumor grade	**P53 staining positive Cases**		**P53 staining negative Cases**	
	No.	**Percentage (%)**	**No.**	**Percentage (%)**
Well differentiated (n=9)	2/9	(22.22)	7/9	(77.77)
Moderately differentiated (n=20)	13/20	(65.00)	7/20	(35.00)
Poorly differentiated (n=5)	4/5	(80.00)	1/5	(20.00)

Table-5: P53 expression in tumor grade of gallbladder carcinoma (n=34)

T:Primary tumor (T-category)

On analysing the p53 expression with tumor grade, p53 expression was observed in 2 out of 9 cases (22.22%) of Well differentiated adenocarcinoma , 13 out of 20 cases (65%) of Moderately differentiated adenocarcinoma and 4 out of 5 cases (80%) of Poorly differentiated adenocarcinoma. Thus, higher p53 expression with increasing grade of gallbladder cancer was observed. (Table-5)

	P53 staining positive Cases		**P53 staining negative Cases**	
	No.	**Percentage (%)**	**No.**	**Percentage (%)**
T1 (n=4)	2/4	(50.00)	2/4	(50.00)
T2 (n=13)	6/13	(46.15)	7/13	(53.84)
T3 (n=16)	11/16	(68.75)	5/16	(31.25)

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

T4 (n=1)	0/1	(00.00)	1/1	(100)
STAGE-1(n=4)	2/4	(50.00)	2/4	(50.00)
STAGE-2 (n=13)	7/13	(53.84)	6/13	(46.15)
STAGE-3 (n=14)	9/14	(64.28)	5/14	(35.71)
STAGE-4 (n=3)	1/3	(33.33)	2/3	(66.66)

Table-6: P53 expression in TNM stage of gallbladder carcinoma (n=34)

T:Primary tumor (T-category)

According to study of the expression of p53 with depth of tumor invasion, out of 4 cases of T1 category, p53 expression was observed in 2 cases (50%) while 6 of 13 cases (46.15%) of T2 category showed p53 expression. Among 16 cases of T3 category p53 positivity was seen in 11 cases (68.75%). P53 positivity was not seen in T4 category.

On analysing the expression of p53 in different stages of diseases, the p53 positivity were 50%, 53.84%, 64.28%, 33.33% in Stage-1, Stage-2, Stage-3 and Stage-4 respectively. (Table-6)

Différentiation grade (n=34)	**P53 staining positive cases**		**P53 staining negative cases**		**Comparison**	**P value**
	No.	**Percentage (%)**	**No.**	**Percentag (%)**		
WD (n=9)	2/9	(22.22)	7/9	(77.77)	WD vs. MD and PD	P=0.050
MD (n=20)	13/20	(65.00)	7/20	(35.00)		
Pd (n=5)	4/5	(80.00)	1/5	(20.00)		

Table 7: Comparative evaluation of P53 expression and adenocarcinoma differentiation grades

WD: Well differentiated adenocarcinoma
MD: Moderately differentiated adenocarcinoma
PD: Poorly differentiated adenocarcinoma

On statistical evaluation, the difference in the level of expression of p53 between tumor grades (WD vs. MD and PD, taken together) was found to be significant (P = 0.050). (TABLE-7)

	P53 staining positive Cases		**P53 staining negative Cases**		**Comparison**	**P Value**
	No.	**Percentage (%)**	**No.**	**Percentage (%)**		
T1 (n=4)	2/4	(50.00)	2/4	(50.00)	T1vsT2-T4	P=0.4079
T2 (n=13)	6/13	(46.15)	7/13	(53.84)		
T3 (n=16)	11/16	(68.75)	5/16	(31.25)		
T4 (n=1)	0/1	(0.00)	1/1	(100)		
STAGE-1(n=4)	2/4	(50.00)	2/4	(50.00)	S1vsS2-S4	P=0.7775
STAGE-2 (n=13)	7/13	(53.84)	6/13	(46.15)		
STAGE-3 (n=14)	9/14	(64.28)	5/14	(35.71)		
STAGE-4 (n=3)	1/3	(33.33)	2/3	(66.66)		

Table 8: **Comparative evaluation of P53 expression with tnm stage of gallbladder carcinoma**

On statistical evaluation of p53 expression with tumor category (T category) and tumor staging, p53 scores showed no significant difference with tumor category (p= 0.4079) and tumor staging (p=0.7775). Thus, correlation of p53 expression was not found with depth of tumor invasion (T category) or tumor stage in our cases. (Table-8)

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

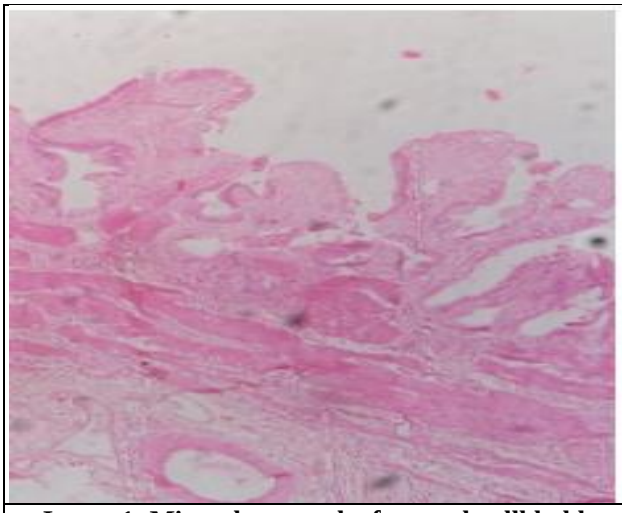

Image 1: Microphotograph of normal gallbladder showing layers of gallbladder wall : mucosa, muscularis and serosa. (H & E 100 x)

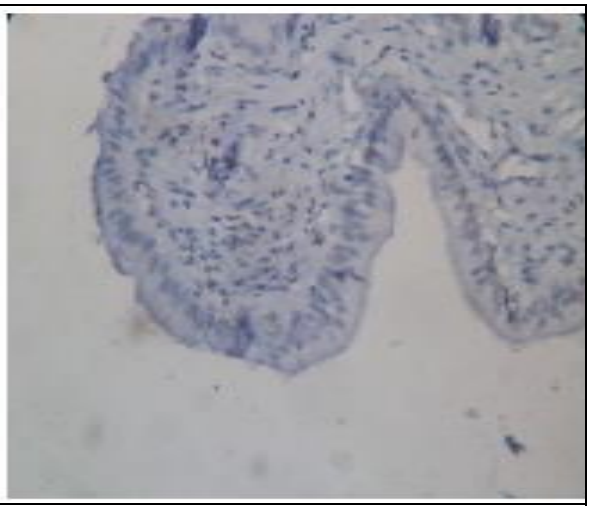

Image 2: Microphotograph of normal gallbladder at 400X showing nuclear p53 negativity.

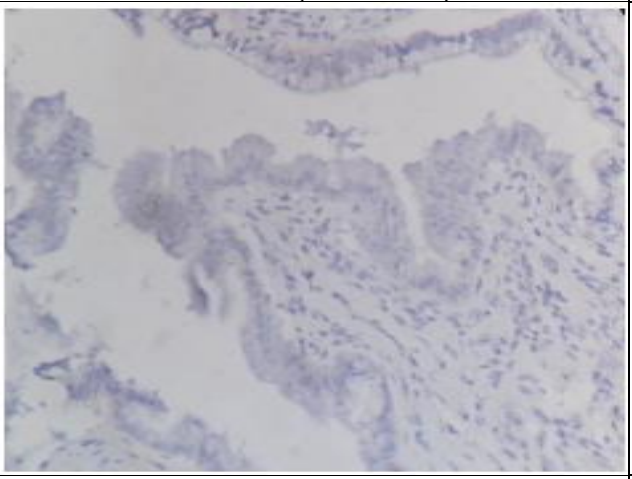

Image 3: Microphotograph (400X) of same case of chronic cholecystitis showing nuclear p53 negativity.

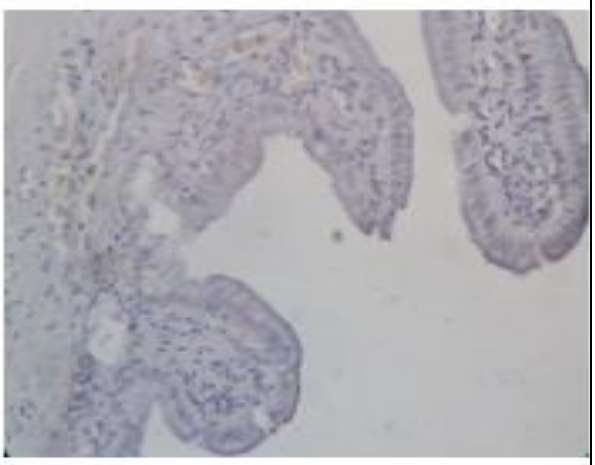

Image 4: Microphotograph of same case (400X) showing nuclear p53 negativity.

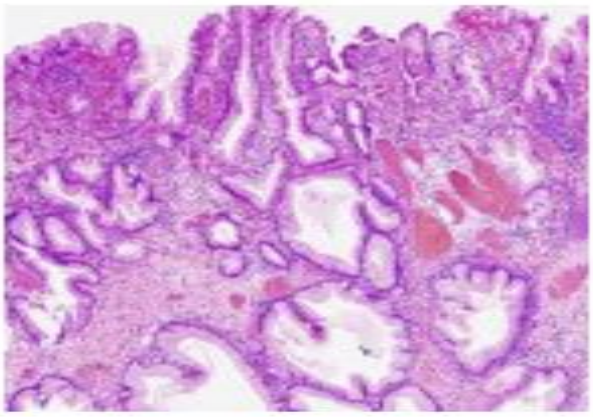

Image 5: H&E stained section (100X) of Chronic cholecystitis with pyloric metaplasia. The pyloric metaplastic glands are lined by tall columnar epithelium with basally located nuclei.

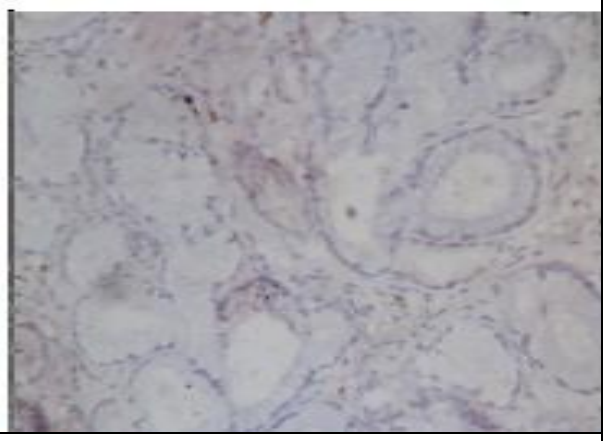

Image 6: High power view (400X) of same case showing nuclear p53 negativity.

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

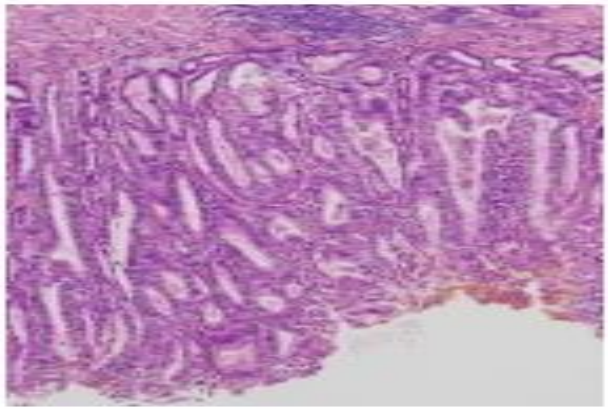	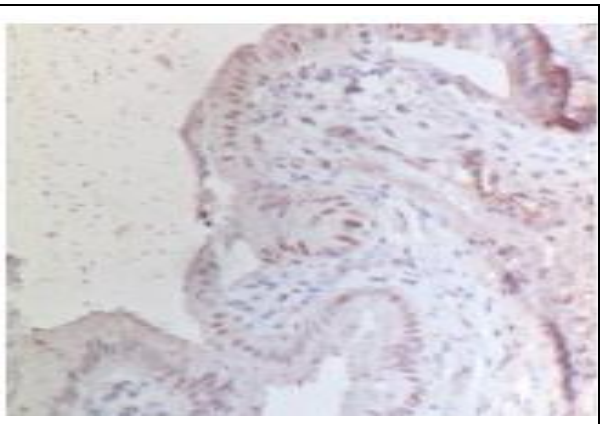
Image 7: H & E stained section (100X) of Well differentiated adenocarcinoma showing large, pleomorphic hyperchromatic nuclei with prominant nucleoli.	**Image : Same case of Well differentiated adenocarcinoma (400X) showing p53 nuclear positivity.**
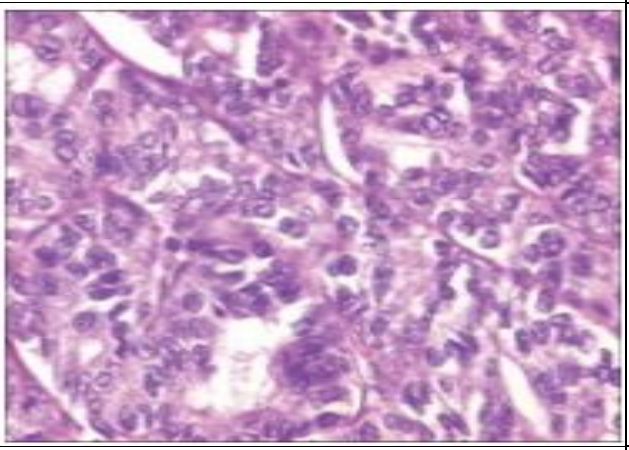	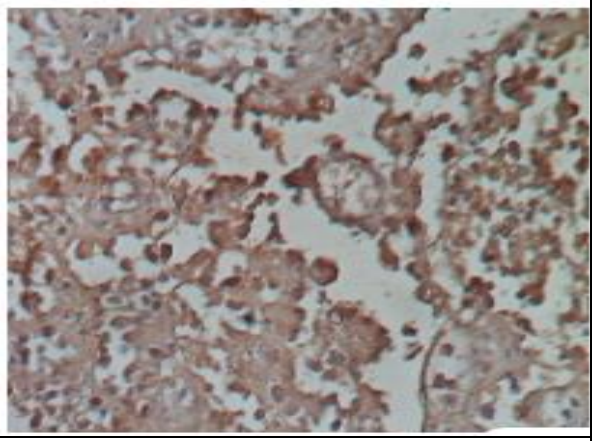
Image 9: H & E stained section (400X) showing Moderately differentiated adenocarcinoma with disturbed glandular architecture, large, pleomorphic hyperchromatic nuclei with prominant nucleoli.	**Image 10: Same case (400X) of Moderately differentiated adenocarcinoma, showing p53 nuclear positivity.**
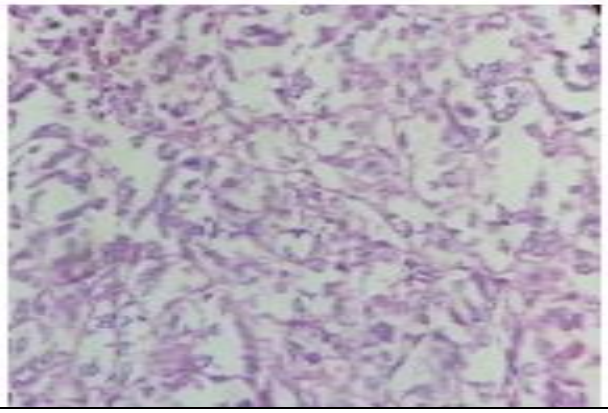	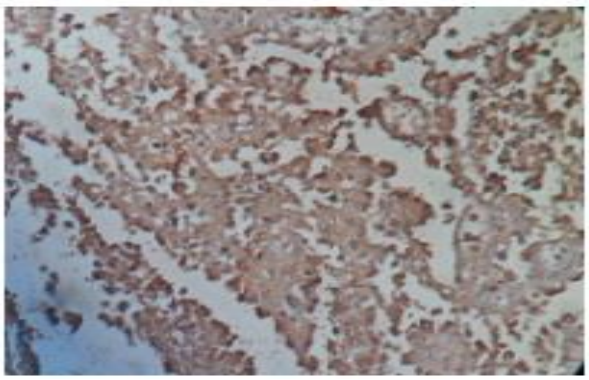
Image 11: H & E stained section (400X) of poorly differentiated adenocarcinoma with loss of glandular architecture, large, pleomorphic hyperchromatic nuclei with prominant nucleoli.	**Image 12: High power view (400X) of same case showing p53 nuclear positivity.**

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

DISCUSSION

A total of 112 cases of gallbladder lesions including 66 cases of chronic cholecystitis and 34 cases of gallbladder adenocarcinoma and 12 specimens of normal gallbladder which served as controls were studied histopathologically and then immunohistochemical analysis for expression of p53 was done. Observations were made in terms of the relationship of p53 expression with tumor differentiation, invasion, nodal involvement, metastasis and stage of the disease.

In context to the cases selected for the study, the age of the total 112 patients ranged from 21-80 years. Among benign group, majority of the cases of chronic cholecystitis (23/66 cases, 34.84%) were found in 41-50 years age group followed by 18/66 (27.27%) in 51-60 years age group. Our findings are in accordance with **Manuela Stancu et al (2007**)[15], **Rakesh B.H. et al (2013)[16] and R. Thamil Selvi et al (2011)**[17]

Among gallbladder cancer cases, maximum number of cases (15 of 34 cases; 44.11%) were in the age group of 51-60 years followed by 26.47% in 61-70 years age group. Majority of cases (85.29%) were seen after the age of 50 years. This data is consistent with data in different literature where it has been found that more than 75% of cases of gallbladder cancer had mean age more than 50 years.

S. Kumar et al (2014)[18], reported most of the patients (75%) in the age group of 51-70 years. In the study of **Khan RA et al (2010)[19]**, the median age of presentation in gallbladder carcinoma was 61 years. **Waghmare RS and Kamal RN (2014)[20],** reported gallbladder cancer after 50 years of age in their study.

Results from our study showed that gallbladder cancer is predominantly a disease of females. Out of 66 cases of chronic cholecystitis, 53 (80.30%) were female and 13 cases (19.69%) were male with female to male ratio of 4:1 while out of 34 cases of gallbladder cancer, 28 cases (82.35%) were females and 06 (17.64%) were males. Male to female ratio was 4.6:1 in gallbladder carcinoma. Incidence of female preponderance in this study are comparable with other studies {**Gupta SC et al (2000)[21] ; Adam R et al (1947)[22]; Glenn F et al (1964)[23]; Khanna R et al (2006)[24]; Aulakh R (2007)[25]; SayeedUnisa et al (2011)[26]; Randi et al (2006)[27] } .**Our findings are in accordance with **Santanu Acharyya et al (2012)[28]** and **Manuela Stancuet al (2007)[15]** who reported female to male ratio of 4:1 in both types of lesions.**Giang T H et al (2012)[29] reported female to male ratio of 4.5:1 in gallbladder carcinoma, similar to our findings.Tyagi et al (1992**)[30], however showed a higher incidence than others with a ratio of 6.5:1.

In the present study, out of total 112 cases, 66 cases (58.9%) were chronic cholecystitis while 34 cases (30.3%) were gallbladder cancer, representing chronic cholecystitis as the common benign lesion. **Manuela Stancu et al (2007)[15]**, analysed 3901 specimens of cholecystectomies and found chronic cholecystitis in 3619 cases (92.8%) and gallbladder cancer in 32 cases (0.8%) revealing chronic cholecystitis as the commonest lesion. **Narang et al (2014)[31]**, also reported chronic cholecystitis as the most common lesion in their study of 200 specimens of cholecystectomies.

Mittal R et al (2010)[32], studied 1312 patients of gallbladder diseases, chronic calculouscholecystitis was seen in 1010 (76.98%) while cancer was observed in 13 patients (0.9%). As mentioned in Sheila Sherlock disease of liver and biliary tract, chronic cholecystitis is the most common gallbladder disease and the same reflection was found in our study. Similarly, **Zahrani and Mansoor (2001)**[33] documented chronic cholecystitis (97%) as the most common lesion.

Out of 66 cases of chronic cholecystitis, hyperplasia was seen in 6.06% cases and 3.03% was associated with pyloric metaplasia .

Manuela Stancuet al (2007)[15] reported hyperplasia in 124 cases (7.8%) of chronic cholecystitis and 86 cases (5%) were associated with metaplasia, predominantly of the pyloric type.

Among malignant lesions, all the 34 cases were reported as Adenocarcinoma, not otherwise specified type, on histopathological examination. Out of these, 34 cases of gallbladder adenocarcinoma, 20 cases (58.82%) were moderately differentiated and, 09 cases (26.47%) were well differentiated and 5 cases (14.7%) were poorly differentiated adenocarcinoma. Most common histological grade was moderately differentiated adenocarcinoma (58.82%).

Our results are comparable with the study of **Veloso MGP et al[34]; Mittal R et al (2010)[32] and Waghmore RS et al (2014)[20].** They also found that moderately differentiated adenocarcinoma was the commonest histopathological grade on microscopic examination.

VelosaMGP et al[34], reported adenocarcinoma, NOS type, in 23/24 cases (95.83%) and the majority were moderately differentiated adenocarcinoma. **Giang TH et al (2011)[29],** also observed adenocarcinoma, NOS type, in most of the cases in their study. Molecular marker **p53** have been identified in gallbladder cancer in very few studies, and in most cases comprising a small number of gallbladder cancer specimens. Thus, their prognostic significance remains to be extensively validated.

In the present study, p53 expression was positive in 19 out of 34 cases (55.88%) while it was not expressed in any case of chronic cholecystitis (0/66 cases) and control gallbladders (0/12 cases).

Our findings are in accordance with study of **Ghosh et al (2013)[12],** who showed p53 expression in 45 of 80 cases (56.25%) of gallbladder cancer. None of the 60

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

cases of chronic cholecystitis and 10 cases control gallbladder tissues expressed p53.

In other studies of gallbladder carcinoma, the p53 protein nuclear expression ranges from 39.6% to 92% of cases,[3-5] similar to our results.

When observed the relation of the level of p53 expression with grade of tumor, low grade tumor (well differentiated) showed expression in 2 of 9 cases (22.22%) while moderately and poorly differentiated adenocarcinoma, expression was observed in 13/ 20 (65%) cases and 4/5 (80%) cases respectively. The level of expression of p53 increased significantly with the grade of the tumor (p=0.05). This is in accordance with the study of **Ghosh et al (2013)[12]** in which low grade tumor (well differentiated) showed low expression of p53 (42.8%) in comparison to that in the moderately differentiated (62.6%) and poorly differentiated tumors (66.7%). Similarly, in **Roa et al(1997)**[13] study, p53 positivity was found in 25% of well differentiated tumor, while moderately or poorly differentiated carcinoma showed 50% positivity.

However, p53 expression did not correlate with depth of the tumor invasion (T classification) and tumor grade. The results of our study corroborate with **Oohashi et al (1995)[35]**, in which p53 overexpression was not related to the level of gallbladder wall invasion by the tumor. These results may indicate that p53 has a role in gallbladder carcinogenesis and in progression of the cancer from low grade to high grade tumor but not in tumor invasiveness. The higher p53 expression with the increasing grade of gallbladder carcinoma suggests its role in tumor progression rather than initiation.

Wee et al (1994)[36], found no correlation of p53 expression with tumor invasion and found p53 over-expression even in dysplasia and carcinoma-in-situ unassociated with invasive malignancy. In present study, dysplasia and non-invasive malignancy was not included but a larger study with few number of such cases will throw light on the role of p53 gene mutation in carcinogenesis.

Oohashi et al (1995)[35], reported p53 over-expression as an early event unrelated to tumor grade, stage, or size etc. P53 expression could thus differentiate benign from malignant lesions of gallbladder.

There are studies indicating that high-grade (poorly differentiated) gallbladder carcinomas tend to over-express p53 protein more than low-grade tumors (well differentiated) but most of these series are too small for statistical Analysis, **Wee et al (1994), Washington et al (1996), Kamel D et al (1993).**[36,37,38] **Kalekou and Miliaras(2004)[39]** found that the expression of p53 protein was significantly higher in deeply invasive tumors (P = 0.028) and in moderately and poorly differentiated carcinomas (P < 0.05).[1]

Kamel et al (1993)[38], raised the hypothesis that p53 is an early event in the carcinogenesis of gallbladder carcinoma. P53 positive dysplasia evolves to a more aggressive type of tumor, which is associated with high tumor grade and p53 positivity.[40]

Roa et al (1997)[13], studied 191 cases of gallbladder carcinoma and similar to our study, they observed increased p53 expression with increasing tumor grade and absence of expression in controls and in normal mucosa adjacent to tumors. **Chang et al (2007)[41],** showed poor survival of gallbladder carcinoma with abnormal p53 expression.

CONCLUSION

P53 expression was positive in 19 out of 34 cases (55.88%) while it was not expressed in any case of chronic cholecystitis (0/66 cases) and control gallbladders (0/12 cases).

The level of expression of p53 increased significantly with the grade of the tumor (p=0.05). P53 expression did not correlate with depth of the tumor invasion (Tclassification) (p=0.4079) and tumor stage (p=0.7775).

These results may indicate that p53 has a role in gallbladder carcinogenesis and in progression of the cancer from low grade to high grade tumor but not in tumor invasiveness. The higher p53 expression with the increasing grade of gallbladder carcinoma suggests its role in tumor progression rather than initiation.

Further studies with large number of cases including an analysis of precancerous lesions and carcinoma in situ will give better insight into the role of these genes in carcinogenesis and progression.

REFERENCES

1. Zatonski, W. A., Lowenfels, A. B., Boyle, P., Maisonneuve, P., Bueno de Mesquita, H. B., Ghadirian, P., Jain, M., Przewozniak, K., Baghurst, P., Moerman, C. J., Simard, A., Howe, G.R., McMichael, A. J., Hsieh, C. C., Walker, A. M. (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. 1997, 89: pp. 1132–38.
2. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, Feuer EJ, Thun MJ Cancer statistics. CA Cancer J Clin ,2005;55:10-30.
3. Zhu AX, Hong TS, Hezel AF, Kooby DA. Current management of gallbladder carcinoma. Oncologist. 2010; 15(2):168-81.
4. Paraskevopoulos JA, Dennison AR, Ross B, Johnson AG. Primary carcinoma of the gallbladder: a 10-year experience. Ann R CollSurgEngl 1992; 74:222.
5. Ghadirian P, Simard A, Baillargeon J. A population-based case-control study of cancer of the bile ducts and gallbladder in Quebec, Canada. Rev EpidemiolSantePublique 1993; 41:107.
6. Miller G and Jarnagin WR: Gallbladder carcinoma. Euro J SurgOncol ,2008;34: 306-312.

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

7. Kuroki T, Tajima Y, Matsuo K, Kanematsu T. Genetic alterations in gallbladder carcinoma. Surg Today, 2005; 35(2):101-5.
8. Lee H, Kim H, Yang H, Kim W. Tumour suppressor gene expression correlates with gastric cancer prognosis. J Pathol. 2003;200:39–46.
9. Galizia G, Ferraraccio F, Lieto E, Orditura M, Castellano P, Imperatore V, et al. Prognostic value of p27, p53, and vascular endothelial growth factor in dukes A and B colon cancer patients undergoing potentially curative surgery. Dis Colon Rectum. 2004;47:1904–14.
10. Alkushi A, Lim P, Coldman A, Huntsman D, Miller D, Gilks C. Interpretation of p53immunoreactivity in endometrial carcinoma: Establishing a clinically relevant cut-off level. Int J GynecolPathol. 2004;23:129–37.
11. Billo P, Marchegiani C, Capella C, Sessa F. [Expression of p53 in gallbladder carcinoma and in dysplastic and metaplastic lesions of the surrounding mucosa]. Pathologica. 2000; 92(4): 249-56.
12. Ghosh M, Sakhuja P, Singh S, Agarwal AK. p53 and beta-catenin expression in gallbladder tissues and correlation with tumor progression in gallbladder cancer. Saudi J Gastroenterol 2013;19:34-9.
13. Roa I, Villaseca M, Araya J, Roa J, de Aretxabala, Melo A, *et al*. p53tumour suppressor gene protein expression in early and advancedgallbladder carcinoma. Histopathology 1997;31:226-30.
14. Puhalla H, Herberger B, Soleiman A, Filipits M, Laengle F, GruenbergerT, *et al*. E-cadherin and beta-catenin expression in normal, inflamed andcancerous gallbladder tissue. Anticancer Res 2005;25:4249-54.
15. Manuela Stancu et al. Romanian Journal of Morphology and Embryology 2007, 48(4):335–342
16. Rakesh B , Rajendra G. A prospective clinicopathological study of 50 cases of chronic calculouscholecystitis in the local population: 2013;12;35:6706-6716.
17. R. Thamil Selvi, Pammy Sinha, P.M. Subramaniam, P.G. Konapur, C.V. Prabha. A clinicopathological study of cholecystitis with special reference to analysis of cholelithiasis. International Journal of Basic Medical Science-July 2011, Vol:2, Issue :2.
18. S K umar , Tiwari A . Evaluation of Microsatellite Instability and Apoptosis in Gall Bladder Malignancy from Patients of a Cohort Exposed to Methylisocyanate. J Carcinog Mutagen 2014:5:171.
19. Rizwan Ahmad Khan, Mohammad Amanullah Khan Advanced presentation of Gallbladder cancer: Epidemioclinicopathological study to evaluate the risk factors and assess the outcome 2010;60:217; 2010.
20. Ramesh S Waghmare, Rima N Kamat. Incidental Gall Bladder Carcinoma in Patients Undergoing Cholecystectomy : A Report of 7 Cases, 2014; 62
21. Gupta SC , Mishra V., Singh PA et al. Gall stone and carcinoma gallbladder. Indian J PatholMicribiol 2000;43:147-154.
22. Adam R, Stranahan A. Cholecystitis and cholelithiasis; an analytical report of 1,104 operative cases. SurgGynecolObstet 1947; 85:776-84.
23. Glenn F, Frey C. Re-evaluation of the treatment of pancreatitis associated with biliary tract diseases. Ann Surg 1964; 160: 723-36.6
24. Khanna R, Chansuria R, Kumar M, Shukla HS. Histological changes in gallbladder due to stone disease. Indian J Surg 2006; 68:201-4.
25. Aulakh R, Mohan H, Attri AK, et al. Comparative study of serum lipid profile and gallstone disease. Indian J PatholMicrobiol 2007; 50:308-12. 29.
26. Sayeed Unisa, Palepu Jagannath, Vinay Dhir, Chiranjeeva Khandelwal, Lalatendu Sarangi, and Tarun Kumar Roy. Population – based study to estimate prevalence and determine risk factors of gallbladder diseases in the rural Gangetic basin of North Indian HPB (Oxford). 2011 February; 13(20):117-125.
27. Randi G, Franceschi S, La Vecchia C. Gallbladder cancer worldwide: geographical distribution and risk factors. Int J Cancer 2006; 118:1591.
28. Santanu Acharyya, Amitabha Chakrobarti, Sourav Sau, Partha Dasgupta, Sandip Ghosh, Anjali Majumdar Incidental Finding of Gall Bladder Carcinoma : A Retrospective Study.2012;116-120
29. Tran H Giang, Tran TB Ngoc and Lewis A Hassell. Carcinoma involving the gallbladder: a retrospective review of 23 cases - pitfalls in diagnosis of gallbladder carcinoma .*Diagnostic Pathology* 2012; 7:10.
30. TyagiSP, Tyagi N, Maheshwari V, Ashraf SM, Sahoo P. Morphological changes in diseased gallbladder: a study of 415 cholecystectomies at Aligarh. (J Indian Med Assoc.1992Jul;90(7):178-81.
31. Dr.Arathi.NA, Seema AwasthiA, Ashutosh KumarA .Pathological Profile Of Cholecystectomies At A Tertiary Centre 2013:2:1;28-38 .
32. Rohin Mittal, Mark Ranjan, Jesudason, SukriaNayak. Selective histopathology in cholecystectomy for gallbladder disease. Indian J Gastroentrol 2010 , 29 (1):32-36.
33. ZahraniIH, Mansoor I. Gallbladder pathologies and cholelithiasis. Saudi Med J. 2001 Oct;22(10):885-9.
34. MoemaGonçalvesPinheiroVeloso, Daniel Nava Rodrigues. Gallbladder carcinoma: clinicopathological study of 24 cases , 2011;vol.47 no.4 Rio de Janeiro.
35. Oohashi Y, Watanabe H, Ajioka Y, Hatakeyama K. p53immunostaining distinguishes malignant from benign lesions of the gall-bladder. PatholInt 1995;45:58-65.
36. Wee A, Teh M, Raju G. Clinical importance of p53 protein in gallbladdercarcinoma and its precursor lesions. J ClinPathol 1994;47:453-6.
37. Washington K, Gottfried M. Expression of p53 in adeno carcinoma ofthe gallbladder and bile ducts. Liver 1996;16:99-104.
38. Kamel D, Paako P, Nuorva K, Vahakangas K, Soini Y. p53 and c-erbB-2 protein expression in adenocarcinomas and epithelial dysplasias of the gallbladder. J Pathol 1993;170:67-72.
39. Kalekou H, Miliaras D. Immunohistochemical study of microvessel density, CD44 (standard form), p53 protein and c-erbB2 in gallbladdercarcinoma. J GastroenterolHepatol 2004;19:812-20.
40. Adson MA. Carcinoma of the gallbladder. SurgClin North Am. 1973; 53(5):1203-16.

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.

DOI: 10.69605/ijlbpr_14.4.2025.163

41. Chang H, Yoo B, Kim S, Lee B, Kim W. Significance of PML and p53 protein as molecular prognostic markers of gallbladder carcinomas. PatholOncol Res 2007;13:326-35.

©2025Int. J. LifeSci.Biotechnol.Pharma.Res.