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P53 EXPRESSION IN THE HISTOPATHOLOGICAL SPECTRUM OF GALLBLADDER LESIONS: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE HOSPITAL, TELANGANA

Histopathology

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ABSTRACT

Background: Gallbladder diseases include a wide spectrum of pathological conditions ranging from inflammatory lesions to malignant tumors. Gallbladder carcinoma is the most common malignancy of the biliary tract and is associated with poor prognosis due to late clinical presentation. Molecular alterations such as mutations in the tumor suppressor gene p53 play an important role in the development and progression of gallbladder carcinoma. Immunohistochemical detection of p53 protein accumulation is widely used as a surrogate marker for p53 gene mutation. **Materials and Methods:** This cross-sectional study was conducted in the Department of Pathology, Osmania Medical College, Hyderabad. A total of 200 cholecystectomy specimens received over a period of two years were included in the study. All specimens were subjected to routine histopathological examination using hematoxylin and eosin staining. Immunohistochemistry for p53 was performed in selected cases. Data regarding age, sex, histopathological diagnosis, presence of gallstones, and p53 expression were analyzed. Statistical analysis was performed using the Chi-square test, and a p-value <0.05 was considered statistically significant. **Results:** Among the 200 cases studied, chronic cholecystitis was the most common lesion (77%), followed by benign lesions (16%), premalignant lesions (1.5%), and gallbladder carcinoma (5.5%). Females constituted the majority of cases (64%). Gallstones were present in 70.5% of cases. p53 positivity was observed in 32 cases (16%). The highest p53 expression was observed in gallbladder carcinoma (72.7%), followed by premalignant lesions (66.6%). Minimal expression was noted in benign and inflammatory lesions. A statistically significant association was observed between p53 expression and histopathological lesions ($p < 0.001$). **Conclusion:** p53 overexpression shows a strong association with malignant and premalignant gallbladder lesions. Immunohistochemical detection of p53 may serve as a useful adjunct marker for identifying early malignant transformation in gallbladder pathology.

KEYWORDS

Gallbladder lesions, p53, Immunohistochemistry, Gallbladder carcinoma, Chronic cholecystitis.

INTRODUCTION

Gallbladder diseases constitute a significant proportion of hepatobiliary pathology and include a wide spectrum of conditions ranging from inflammatory disorders to benign and malignant tumors. Chronic cholecystitis associated with cholelithiasis is the most common pathology encountered in cholecystectomy specimens. Gallbladder carcinoma is the most common malignancy of the biliary tract and represents one of the most aggressive gastrointestinal cancers. It is characterized by rapid progression, early invasion, and poor prognosis. The disease often remains clinically silent in early stages and is frequently diagnosed incidentally following cholecystectomy performed for presumed benign gallbladder disease.
Several risk factors have been implicated in the development of gallbladder carcinoma, including chronic cholelithiasis, chronic inflammation, female gender, increasing age, and certain environmental and genetic factors. Chronic inflammation caused by gallstones is believed to play a crucial role in gallbladder carcinogenesis by inducing repeated epithelial injury and regeneration.

The development of gallbladder carcinoma is thought to occur through a multistep sequence involving chronic inflammation, epithelial metaplasia, dysplasia, and eventual malignant transformation. During this process, various molecular genetic alterations accumulate, leading to uncontrolled cellular proliferation and tumor development.

Among these molecular alterations, mutations in the TP53 tumor suppressor gene are one of the most frequently reported abnormalities in gallbladder carcinoma. The p53 protein is a key regulator of the cell cycle and plays an important role in maintaining genomic stability by inducing cell cycle arrest, DNA repair, or apoptosis in response to cellular stress.

Mutation of the TP53 gene leads to production of a dysfunctional p53 protein with prolonged half-life, resulting in its accumulation within the cell nucleus. This abnormal protein accumulation can be detected using immunohistochemistry, making p53 immunostaining a useful surrogate marker for underlying genetic alterations. Previous studies have demonstrated that p53 overexpression is significantly more common in gallbladder carcinoma compared to benign gallbladder lesions. Furthermore, increased p53 expression has been observed in premalignant lesions, suggesting that TP53 mutation may occur early in gallbladder carcinogenesis.

Evaluation of p53 expression across the histopathological spectrum of gallbladder lesions may therefore provide valuable insight into the molecular mechanisms involved in gallbladder carcinogenesis and may assist in identifying lesions at risk of malignant transformation.

The present study was undertaken to evaluate the histopathological spectrum of gallbladder lesions in cholecystectomy specimens and to assess the pattern of p53 immunohistochemical expression in inflammatory, benign, premalignant, and malignant gallbladder lesions.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Pathology, Osmania Medical College, Hyderabad. The study included 200 cholecystectomy specimens received over a period of two years.

Inclusion Criteria

All cholecystectomy specimens received during the study period were included.

Exclusion Criteria

Autolyzed specimens and samples with inadequate tissue were excluded from the study.

Histopathological Examination

All specimens were fixed in 10% neutral buffered formalin. Gross examination was performed to evaluate the size, wall thickness, mucosal appearance, presence of gallstones, and any mass lesions.

Representative sections were taken from the fundus, body, neck, and any abnormal areas. Tissue sections were processed routinely, embedded in paraffin, and stained with hematoxylin and eosin (H&E) for microscopic examination.

Histopathological diagnoses were categorized into:

- Inflammatory lesions

- Benign non-neoplastic lesions
- Premalignant lesions
- Malignant lesions

Immunohistochemistry
Immunohistochemical staining for p53 was performed in selected cases including premalignant and malignant lesions.

Paraffin sections of 3–4 µm thickness were mounted on poly-L-lysine coated slides. Following deparaffinization and rehydration, antigen retrieval was performed using heat-induced epitope retrieval. Endogenous peroxidase activity was blocked before incubation with primary monoclonal anti-p53 antibody.

Detection was carried out using secondary antibody and DAB chromogen. Sections were counterstained with hematoxylin.

Nuclear staining in epithelial cells was considered positive for p53 expression.

Statistical Analysis
Data were entered in Microsoft Excel and analyzed using statistical methods. The Chi-square test was used to determine association between p53 expression and different gallbladder lesions. A p-value <0.05 was considered statistically significant.

RESULTS
A total of 200 cholecystectomy specimens were included in the present study.

Age and Sex Distribution
The majority of patients belonged to the 40–60 years age group, with a mean age of approximately 47.8 years.

Females constituted 64% of cases, while males accounted for 36%, demonstrating a clear female predominance.

Histopathological Spectrum
The most common lesion observed was chronic cholecystitis, accounting for 154 cases out of 200 cases (77%).

Other lesions included:
- Benign non-neoplastic lesions – 32 cases out of 200 cases (16%)
- Premalignant lesions – 3 cases out of 200 cases (1.5%)
- Gallbladder carcinoma – 11 cases out of 200 cases (5.5%)

Thus, non-neoplastic lesions constituted the majority of gallbladder specimens.

Association with Gallstones
Gallstones were present in 141 cases out of 200 (70.5%), demonstrating a strong association between gallstone disease and gallbladder pathology.

p53 Immunohistochemical Expression
p53 positivity was observed in 32 cases (16%), while 168 cases (84%) were negative for p53 expression.

Among the positive cases:
- Chronic cholecystitis – 15 cases out of 154 cases
- Benign lesions – 8 cases out of 32 cases
- Premalignant lesions – 2 cases out of 3 cases
- Gallbladder carcinoma – 8 cases out of 11 cases

The highest proportion of p53 positivity was observed in gallbladder carcinoma, where 72.7% of cases demonstrated positive staining.

Statistical analysis showed a highly significant association between p53 expression and histopathological lesion type ($p < 0.001$).

DISCUSSION
Gallbladder diseases represent a wide spectrum of pathological conditions ranging from inflammatory disorders to invasive carcinoma. In the present study, chronic cholecystitis was the most common lesion encountered in cholecystectomy specimens.

This finding is consistent with previous studies, which have reported chronic inflammatory changes as the predominant pathology in gallbladder specimens. The high prevalence of chronic cholecystitis can be attributed to the strong association between gallstones and chronic inflammation.

The present study demonstrated a clear female predominance, which is consistent with earlier studies. Hormonal factors, particularly estrogen are believed to influence bile composition and contribute to gallstone formation, thereby increasing the risk of gallbladder disease in females.

Gallstones were present in more than three-fourths of the cases in this study, further supporting the well-established relationship between cholelithiasis and gallbladder pathology.

The role of molecular alterations in gallbladder carcinogenesis has been widely investigated in recent years. Among these alterations, mutation of the TP53 gene has been identified as one of the most frequent genetic abnormalities in gallbladder carcinoma.

In the present study, p53 expression was significantly higher in malignant and premalignant lesions compared with benign lesions. The highest positivity was observed in gallbladder carcinoma.

Similar findings were reported by Roa et al., who demonstrated increased p53 expression in gallbladder carcinoma compared to benign lesions.

Doval et al. also reported progressive increase in p53 expression from dysplasia to carcinoma, supporting the concept of multistep carcinogenesis.

The progressive increase in p53 expression observed in this study from inflammatory lesions to premalignant lesions and carcinoma supports the hypothesis that TP53 mutation plays an important role in the development and progression of gallbladder carcinoma.

Although p53 expression was occasionally observed in chronic cholecystitis, the frequency was significantly lower compared with malignant lesions. This may represent early molecular alterations occurring in chronically inflamed gallbladder mucosa.

Overall, the findings of the present study highlight the potential role of p53 immunohistochemistry as a useful adjunct marker in identifying premalignant and malignant gallbladder lesions.

CONCLUSION
The present study demonstrated that chronic cholecystitis is the most common gallbladder lesion encountered in cholecystectomy specimens. Gallbladder carcinoma constituted a smaller but clinically significant proportion of cases.

p53 overexpression was significantly associated with malignant and premalignant gallbladder lesions. The results support the role of p53 mutation in gallbladder carcinogenesis.

Immunohistochemical evaluation of p53 may serve as a useful adjunct tool in identifying early malignant transformation and improving diagnostic accuracy in gallbladder pathology.

Further studies with larger sample sizes and molecular analysis are recommended to better understand the role of p53 in gallbladder carcinogenesis.

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