RESEARCH ARTICLE

The diagnostic value of cyclin d1, EGFR, P53 and Ki-67 in epithelial dysplasi of the gallbladder

Ozgen Arslan Solmaz[1], Mumin Emiroglu[2], Mehmet Bugra Bozan[3]

Abstract

Objective: To quantitatively compare the expression levels of cyclin D1, epidermal growth factor receptor, Kiel-67 antigen and tumour suppressor protein P53 between gallbladder flat dysplasia and reactive epithelial changes.

Method: The retrospective, analytical, cross-sectional study was conducted from November 1, 2024, to January 5, 2025, at the Department of Pathology, Health Sciences University, Elazıg Fethi Sekin City Hospital, Elazıg, Türkiye, and comprised cholecystectomy specimens collected between September 2010 and October 2024. Immunohistochemical staining was performed for cyclin D1, epidermal growth factor receptor, Kiel-67 antigen and tumour suppressor protein P53. Staining intensity and percentage were analysed using histoscore calculations. Data was analysed using SPSS 20.

Results: Of the 10,509 specimens reviewed, 211(2%) were analysed; 159(75.4%) females and 52(24.6%) males with overall mean age 52.34 ±15.43 years (range: 16-87 years). There were 118(55.9%) cases of reactive epithelial changes and 93(44.1%) cases of flat dysplasia. Significant differences were observed between the groups with respect to age, epidermal growth factor receptor staining intensity, cyclin D1 staining percentage and intensity, and Kiel-67 proliferation index (p<0.001). Cyclin D1 staining percentage, intensity and Kiel-67 expression were markedly higher in dysplastic cases, underscoring their potential diagnostic value (p<0.001). Although epidermal growth factor receptor staining intensity was significantly elevated in dysplasia (p<0.001), its staining percentage did not exhibit diagnostic significance (p=0,261). Tumour suppressor protein P53 expression showed no significant difference between reactive and dysplastic lesions (p=0.44).

Conclusion: Cyclin D1, epidermal growth factor receptor and Kiel-67 were found to be useful biomarkers for distinguishing gallbladder dysplasia from reactive epithelial changes, whereas tumour suppressor protein P53 showed limited diagnostic value.

Keywords: Gallbladder neoplasms, Reactive changes, Cyclin D1, Ki-67 Antigen, Receptor, Epidermal growth factor, Tumour suppressor protein P53. (JPMA 76: 1292; 2026) **DOI: https://doi.org/10.47391/JPMA.30295**

Introduction

Gallbladder epithelial lesions comprise a broad spectrum, ranging from reactive epithelial alterations to premalignant and malignant conditions, including metaplasia and dysplasia. Dysplasia and metaplasia are recognised precursor lesions of gallbladder carcinoma and are, therefore, of considerable pathological importance. Given the frequent evaluation of cholecystectomy specimens in routine practice, such epithelial alterations are commonly encountered by pathologists.[1] Inflammatory conditions such as gallstones, parasitic infections and sclerosing cholangitis may induce reactive epithelial changes, which often mimic dysplasia and complicate histopathological diagnosis.[2] Accurate identification of precursor lesions is essential, as dysplasia may be associated with synchronous or subsequent malignancy within the biliary tract.[3,4]

[1,2]Department of Pathology, University of Health Sciences, Fethi Sekin City Hospital, Elazig, Turkiye; [3]Department of General Surgery, University of Health Sciences, Fethi Sekin City Hospital, Elazig, Turkiye.

Correspondence: O.A. Solmaz. e-mail: ozgensolmaz_73@hotmail.com

ORCID ID: 0000-0002-8942-199X

Submission completed: 15-05-2025 **1st Revision received:** 19-08-2025

Acceptance: 01-04-2026 **Last Revision received:** 31-03-2026

Dysplasia is a premalignant lesion with a reported incidence of approximately 3.3%.[1] According to the World Health Organisation (WHO) classification, gallbladder dysplasia is categorised as biliary intraepithelial neoplasia grades 1-3 (BilIN 1-3); however, practical distinction between dysplasia and reactive epithelial changes remains challenging, particularly in non-tumoural flat lesions.[5,6] Flat dysplasia is characterised by subtle architectural and cytological abnormalities, including nuclear elongation, pseudostratification and mild hyperchromasia, which may overlap considerably with inflammation-related reactive changes and complicate diagnosis.[7]

In the absence of specific clinical, radiological or gross pathological findings, the diagnosis of gallbladder flat dysplasia relies predominantly on microscopic evaluation. Nevertheless, morphological assessment alone may be insufficient in borderline cases, highlighting the need for additional diagnostic tools.[4] In recent years, studies have focused on immunohistochemical (IHC) biomarkers related to cell cycle regulation and cellular proliferation in gallbladder dysplasias.[8]

Biomarkers such as epidermal growth factor receptor

(EGFR), Kiel-67 antigen, tumour suppressor protein P53 and cyclin D1 are widely used IHC markers that reflect cellular proliferation and cell cycle alterations, and may support the differential diagnosis of epithelial lesions, including gallbladder dysplasia.[8] Evaluating the expression profiles of these markers may, therefore, assist in distinguishing dysplastic lesions from reactive epithelial changes and improve diagnostic accuracy in challenging gallbladder lesions.[9,10]

The current study was planned to assess the diagnostic utility of EGFR, Ki-67, P53 and cyclin D1 expression in differentiating gallbladder flat dysplasia from reactive epithelial changes.

Materials and Methods

The retrospective, analytical, cross-sectional study was conducted from November 1, 2024, to January 5, 2025, at the Department of Pathology, Health Sciences University, Elazıg Fethi Sekin City Hospital, Elazıg, Türkiye, and comprised cholecystectomy specimens collected between September 2010 and October 2024. Data was retrieved from the institutional pathology information system, and the cases were identified by searching the diagnosis section using the term "gallbladder". All the samples were formalin-fixed, paraffin-embedded, and sectioned at a thickness of 3µm for haematoxylin and eosin (H&E) staining.

The cases included were those with complete clinical and histopathological data and formalin-fixed, paraffin-embedded tissue samples of sufficient quality for IHC evaluation. The samples excluded were those exhibiting tissue autolysis, poor fixation, or marked artefactual distortion that could interfere with IHC staining and interpretation. Additionally, samples with incomplete data or insufficient remaining tissue were excluded.

A single pathologist evaluated the slides using a light-emitting diode (LED) microscope (Model: DM2000 LED; Leica Microsystems CMS GmbH, Wetzlar, Germany). Initial diagnoses were confirmed, and the cases showing cells with pleomorphic, mildly hyperchromatic nuclei and loss of polarity, differing from normal epithelium, were classified as reactive changes. Flat dysplasia diagnosis was based on the presence of a flat growth pattern on the surface, increased cellular alignment, hyperchromatic and elongated nuclei localised basally and a prominent cytoplasmic band on the surface.

The sample size was determined using priori power analysis for the comparison of two independent group means, using standard sample size calculation formulas. A medium effect size was defined as Cohen's d=0.50, representing the expected difference between the means of two independent groups with significance level (α) 0.05 and statistical power (1-beta [β]) 0.80.[11] The sample was raised using non-probabilistic consecutive sampling technique. Paraffin blocks from the cases analysed were mounted onto positively charged slides.

IHC staining was performed using peroxidase-based methods with EGFR, cyclin D1, P53 and Ki-67. Sections were deparaffinised with xylene, rehydrated through graded alcohols, and washed in distilled water. Antigen retrieval was performed in sodium citrate solution with potential of hydrogen (pH) 6.0 using heat, followed by blocking endogenous peroxidase activity with 3% hydrogen peroxide (H_2O_2) solution. the sections were incubated with appropriate primary antibodies to allow binding to specific target proteins. After applying secondary biotinylated antibodies, a peroxidase-conjugated streptavidin solution was added, and the reaction was developed using 3,3'-diaminobenzidine (DAB) chromogen solution. Counterstaining with haematoxylin completed the process (Figure 1).

EGFR expression was evaluated based on membranous staining observed through IHC methods. Staining intensity

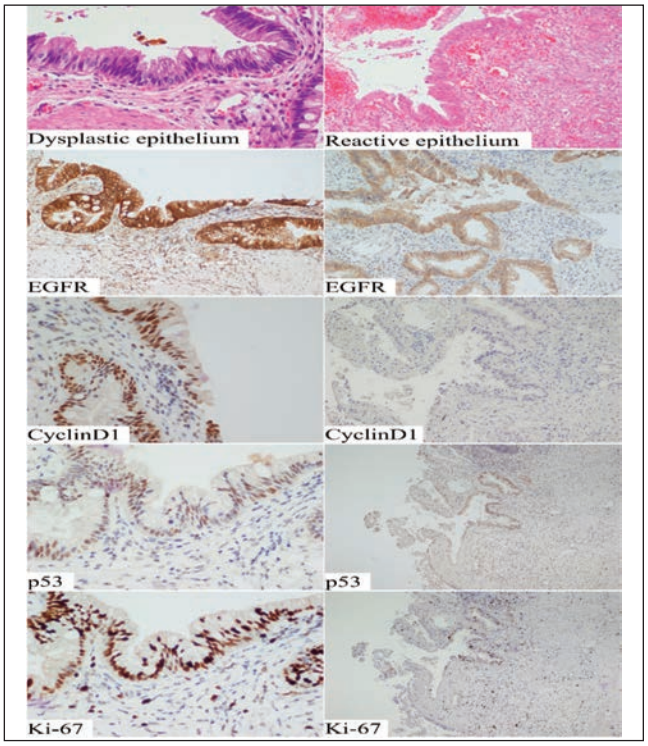

Figure-1: Immunohistochemical staining of EGFR, cyclin D1, Ki-67 and P53 in both reactive and dysplastic cases. The images illustrate the differential expression patterns of these markers, aiding in the distinction between reactive atypia and dysplasia.

EGFR: Epidermal growth factor receptor, Ki-67: Kiel-67, P53: Tumour suppressor protein P53.

was classified based on the level of staining observed on cell membranes. Cases with no staining were classified as '0' (negative). Cells showing weak membranous staining were categorised as '1+' (weak). Cases with distinct but incomplete membranous staining were classified as '2+' (moderate), and cases exhibiting strong and complete membranous staining were evaluated as '3+' (strong). Additionally, classification was performed based on the percentage of stained cells. Cases with a positive staining percentage of 0-10% were categorised as 'negative', those with 10-50% as 'moderate' and cases with >50% as 'high'. After recording the results, the histoscore (H-score) was calculated using the formula; H-score = staining intensity × staining percentage.[9,12]

Cyclin D1 expression was evaluated based on positive nuclear staining. Scoring was performed based on the percentage of cells exhibiting nuclear staining, with 0 = no staining, 1 = staining in <10% cells, 2 = staining in 10-50% cells, and 3 = staining in >50% cells. Additionally, staining intensity was graded as 0 = no staining, grade 1 = weak, grade 2 = moderate and grade 3 = strong. After recording the results, the H-score was calculated.[13,14]

P53 expression was evaluated based on nuclear staining, and was classified as either wild type or mutant type. If the staining pattern was low or limited to focal areas, it was considered 'wild type'. Conversely, diffuse positivity in nearly all cells or the absence of any staining (null pattern) was classified as 'mutant type'.[15]

For the Ki-67 proliferation index, the number of nuclear-positive cells was counted among 1,000 tumour cells. This count was performed at 400X magnification using a microscope (Model: DM2000 LED; Leica Microsystems CMS GmbH, Wetzlar, Germany). If the proportion of Ki-67-positive cells was >20%, it was classified as a high proliferation index, whereas a proportion of <20% was considered a low proliferation index .[16]

Data was analysed using SPSS 20. Data normality of continuous variables was assessed using the Shapiro-Wilk test. Age demonstrated a normal distribution and was analysed using the student's *t*-test, whereas EGFR, cyclin D1 and Ki-67 H-scores showed non-normal distributions and were analysed using the Mann-Whitney U test. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. P<0.05 was considered statistically significant.

Results

Of the 10,509 specimens reviewed, 211(2%) met the inclusion criteria. Ther were 159(75.4%) females and 52(24.6%) males, and the overall mean age was 52.34±15.43 years (range: 16-87 years). There were 118(55.9%) cases of reactive epithelial changes and 93(44.1%) cases of flat dysplasia. Significant differences were observed between the groups with respect to EGFR staining intensity, cyclin D1 staining percentage and intensity, and Ki-67 proliferation index (p<0.001) (Table 1) (Figure 2).

No significant difference was observed between the

Table-1: Distribution of reactive atypia and dysplasia cases based on EGFR staining intensity, EGFR staining percentage, cyclin D1 staining percentage, cyclin D1 staining intensity, P53 mutation type, and Ki-67 proliferation index.

		Cases [n (%)]		Total [n (%)]	*p*-value
		Reactive atypia	Displasia		
EGFR stainig intensity	Negative	6 (2.8)	3 (1.4)	9 (4.3)	<0.001
	Weak	104 (49.3)	55 (26.1)	159 (75.4)	
	Moderate	8 (3.8%)	33 (15.6)	41 (19.4)	
	Strong	0 (0)	2 (0.9)	2 (0.9)	
Total	118 (55.9)	93 (44.1)	211 (100)		
EGFR staining percentage	0-10%	6 (2.8)	3 (1.4)	9 (4.3)	0.261
	10-50%	69 (32.7)	46 (21.8)	115 (54.5)	
	>50%	43 (20.4)	44 (20.9)	87 (41.2)	
Total	118 (55.9)	93 (44.1)	211 (100)		
CyclinD1 staining percentage	Score 0	89 (42.2)	3 (1.4)	92 (43.6)	<0.001
	Score 1	29 (13.7%)	44 (20.9)	73 (34.6)	
	Score 2	0 (0%)	36 (17.1)	36 (17.1)	
	Score 3	0 (0)	10 (4.7)	10 (4.7)	
Total	118 (55.9)	93 (44.1)	211 (100)		
CyclinD1 staining intensity	Negative	89 (42.2)	3 (1.4)	92 (43.6)	<0.001
	Weak	28 (13.3)	60 (28.4)	88 (41.7)	
	Moderate	1 (0.5)	26 (12.3)	27 (12.8)	
	Strong	0 (0)	4 (1.9)	4 (1.9%)	
Total	118 (55.9)	93 (44.1)	211 (100)		
P53	Wild	118 (55.9)	92 (43.6)	210 (99.5)	0.441
	Mutant	0 (0)	1 (0.5)	1 (0.5)	
Total	118 (55.9)	93 (44.1)	211 (100)		
Ki67	Low Ki-67 index	118 (55.9)	54 (25.6)	172 (81.5)	<0.001
	High Ki-67 index	0 (0)	39 (18.5)	39 (18.5)	
Total	118 (55.9)	93 (44.1)	211 (100)		

EGFR: Epidermal growth factor receptor, Ki-67: Kiel-67, P53: Tumour suppressor protein P53.

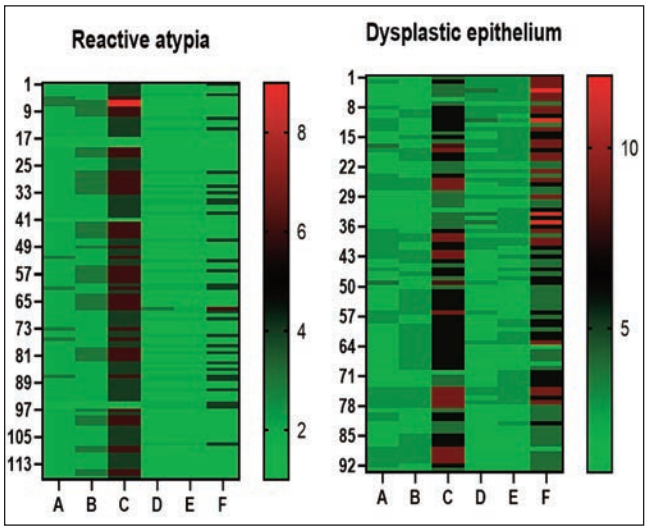

Figure-2: Heatmap showing immunohistochemical expression patterns in reactive epithelial changes and flat dysplasia cases. The Y-axis lists individual cases and the X-axis indicates the immunohistochemical markers. Colour intensity reflects expression levels (green: low; red: high) based on H-score values. The left panel represents reactive epithelial changes, and the right panel represents flat dysplasia.

Table-2: Clinicopathological and immunohistochemical characteristics of flat dysplasia and reactive epithelial changes.

Variable	**Reactive epithelial changes** (n = 118)	**Flat dysplasia** (n = 93)	***p*-value**
Mean Age (years)	48.1±15.0	57.8±14.3	<0.001
Gender (female/male), n (%)	89/29 (75.4/24.6)	70/23 (75.3/24.7)	0.99
Mean EGFR H-score	4.7±1.4	5.8±2.0	<0.001
Cyclin D1 H-score, median (IQR)	1.0 (0.75)	6.0 (5.0)	<0.001

EGFR: Epidermal growth factor receptor, SD: Standard deviation, IQR: Interquartile range.

reactive epithelial change and flat dysplasia groups in terms of gender distribution (p=0.979). Patients with flat dysplasia were significantly older than those with reactive epithelial changes (p<0.001). Significantly higher EGFR and cyclin D1 H-scores were noted in the flat dysplasia group compared to the reactive epithelial change group (p<0.001) (Table 2). (Figure 2).

Discussion

The current study's findings highlight that cyclin D1, EGFR and Ki-67 serve as significant markers in distinguishing reactive epithelial changes from flat dysplasia in gallbladder epithelium.

Cyclin D1 is a key protein involved in the gap-1 (G1) to synthesis (S) phase transition of the cell cycle and the regulation of cell proliferation.[13] A study on gallbladder epithelial dysplasia found no cyclin D1 expression in non-neoplastic epithelium, whereas progressive cyclin D1 expression was observed in the dysplasia-to-carcinoma sequence.[16] The overexpression of cyclin D1 reflects increased cellular proliferation and uncontrolled progression of the cell cycle, indicating a higher susceptibility to malignant transformation. This suggests that both the staining intensity and staining percentage of cyclin D1 are important diagnostic parameters. Consequently, H-index assessment may be used more frequently in clinical decision-making processes for this marker.

Ki-67 is a marker that directly reflects cell proliferation and is frequently used to assess tumour aggressiveness.[17] In the current study, the significant difference in Ki-67 expression between reactive changes and dysplasia confirms its reliability in measuring proliferative activity. The high level of Ki-67 expression in dysplastic lesions suggests increased proliferative capacity and potential malignancy.[1] In a study, high Ki-67 expression was observed in 5% of cases with reactive changes and 20% of dysplasia.[17] Another study reported high Ki-67 expression in 38% of dysplasia cases and 8% of cases with reactive changes.[18] Contrary to these findings, a study observed low Ki-67 expression in all dysplasia cases, reactive changes and 75% of carcinomas.[19] Despite such variability, Ki-67 emerges as an important marker that could serve as a diagnostic differentiator, particularly between dysplasia and reactive changes.

In the current study, EGFR expression was observed in both groups, but staining intensity was higher in dysplastic cases. EGFR is a receptor tyrosine kinase that plays a critical role in cell growth and proliferation.[20] Previous studies have reported that EGFR shows high expression, particularly in advanced-stage adenocarcinomas, but its role in dysplasia is not significant.[21] In a study, weak to moderate EGFR expression was observed in dysplasia cases, while weak staining was reported in 64% of inflammatory lesions.[22] In another study, 85.7% of dysplasia cases showed EGFR overexpression, whereas no staining was observed in normal tissues. The current findings indicate that while EGFR staining intensity may have limited value in distinguishing between reactive and dysplastic lesions, the staining percentage does not exhibit a significant difference. In the H-index assessment of EGFR, it was observed that while staining intensity was significantly higher in dysplasia, the staining percentage did not show a diagnostic difference. This suggests that the role of EGFR in early-stage gallbladder lesions may be limited, but could become more pronounced in later stages.

P53 is a tumour suppressor protein that plays a crucial role in cell cycle regulation and apoptotic mechanisms.[23,24] In the current study, P53 expression did not show a statistically significant difference between reactive changes and dysplasia. This finding suggests that P53 is not a reliable diagnostic marker for distinguishing dysplasia.

Similarly, a study reported no significant difference in P53 expression between reactive gallbladder epithelium and dysplastic epithelium, consistent with the current findings. However, P53 overexpression was present in malignant lesions, indicating its potential utility as a diagnostic marker in differentiating malignant from benign lesions.[25] In contrast, a study observed wild-type P53 staining in normal and reactive epithelium, while mutant overexpression was detected in dysplastic cases.[26] P53 appears to have limited utility as a marker for distinguishing dysplasia from reactive changes. Instead, it holds greater clinical significance in the context of invasive malignancy.

The current study has limitations owing to its retrospective design and a relatively small sample size. Future research should focus on prospective, large-scale studies and molecular profiling to further validate these findings and explore their prognostic and therapeutic implications in gallbladder tumourigenesis.

Conclusion

Cyclin D1, Ki-67 and EGFR were found to be promising diagnostic biomarkers for differentiating dysplasia from reactive changes in gallbladder lesions. These markers could aid in overcoming diagnostic challenges, guiding more accurate histopathological evaluations.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Esendağlı G, Akarca FG, Balcı S. A retrospective evaluation of the epithelial changes/lesions and neoplasms of the gallbladder in Turkey and a review of the existing sampling methods: a multicentre study. Turk Patoloji Derg 2018;34:41-48. doi: 10.5146/tjpath.2017.01404.
2. Adsay NV, Basturk O. Dysplasia and early carcinoma of the gallbladder and bile ducts: terminology, classification and significance. Gastroenterol Clin North Am 2024;53:85-108. doi: 10.1016/j.gtc.2023.10.001.
3. Roa JC, Basturk O, Adsay V. Dysplasia and carcinoma of the gallbladder: pathological evaluation, sampling, differential diagnosis and clinical implications. Histopathology 2021;79:2-19. doi: 10.1111/his.14360.
4. Koshiol J, Bellolio E, Vivallo C, Cook P, Roa JC, McGee EE, et al. Distribution of dysplasia and cancer in the gallbladder: an analysis from a high cancer-risk population. Hum Pathol 2018;82:87-94. doi: 10.1016/j.humpath.2018.07.015.
5. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, et al. WHO Classification of Tumours Editorial Board. The 2019 WHO classification of tumours of the digestive system. Histopathology 2020;76:182-88. doi: 10.1111/his.13975.
6. Katabi N. Neoplasia of gallbladder and biliary epithelium. Arch Pathol Lab Med 2010;134:1621-7. doi: 10.5858/2009-0580-RAR.1.
7. Agarwal A, Bansal R, Gupta M. A study of Cyclin D1, E-cadherin, EGFR, HER-2, Ki67 and P53 tumour marker expressions in neoplastic and non-neoplastic gallbladder lesions and their clinicopathological correlation. Int J Med Sci Diagn Res 2022;6:6-21. doi: 10.32553/ijmsdr.v6i11.958.
8. Doval DC, Azam S, Sinha R, Batra U, Mehta A. Expression of epidermal growth factor receptor, P53, Bcl2, vascular endothelial growth factor, cyclooxygenase-2, cyclin D1, human epidermal receptor-2 and Ki-67: association with clinicopathological profiles and outcomes in gallbladder carcinoma. J Carcinog 2014;13:10. doi: 10.4103/1477-3163.139450.
9. Tchakarska G, Sola B. The double dealing of cyclin D1. Cell Cycle 2020;19:163-78. doi: 10.1080/15384101.2019.1706903.
10. Kaufman M, Mehrotra B, Limaye S, White S, Fuchs A, Lebowicz Y, et al. EGFR expression in gallbladder carcinoma in North America. Int J Med Sci 2008;5:285-91. doi: 10.7150/ijms.5.285.
11. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale (NJ): Lawrence Erlbaum Associates; 1988.
12. Peurala E, Koivunen P, Haapasaari KM, Bloigu R, Jukkola-Vuorinen A. The prognostic significance and value of cyclin D1, CDK4 and p16 in human breast cancer. Breast Cancer Res 2013;15:R5. doi: 10.1186/bcr3376.
13. Ahmed ES, Elnour LS, Hassan R, Siddig EE, Chacko ME, Ali ET, et al. Immunohistochemical expression of Cyclin D1 among Sudanese patients diagnosed with benign and malignant prostatic lesions. BMC Res Notes 2020;13:295. doi: 10.1186/s13104-020-05138-7.
14. Januszewicz W, Pilonis ND, Sawas T, Phillips R, O'Donovan M, Miremadi A, et al. The utility of P53 immunohistochemistry in the diagnosis of Barrett's oesophagus with indefinite for dysplasia. Histopathology 2022;80:1081-90. doi: 10.1111/his.14642.
15. Nakanishi Y, Zen Y, Kondo S, Itoh T, Itatsu K, Nakanuma Y. Expression of cell cycle-related molecules in biliary premalignant lesions: biliary intraepithelial neoplasia and biliary intraductal papillary neoplasm. Hum Pathol 2008;39:1153-61. doi: 10.1016/j.humpath.2007.11.018.
16. Gupta A, Gupta S, Rajput D, Durgapal P, Chennatt JJ, Kishore S, et al. Expression and clinicopathological correlation of Ki-67 in gallbladder carcinoma. J Carcinog 2021;20:11. doi: 10.4103/jcar.JCar_9_21.
17. Ramesh O, Gupta M, Kaushik S, Acharya S, Thakur B, Bhardwaj A. Study of morphology with assessment of expression of proliferation marker Ki67 antigen and P53 protein in lesions of gall bladder. Indian J Pathol Microbiol 2024;67:367-73. doi: 10.4103/ijpm.ijpm_463_22.
18. Salman SS, Raziq AH, Ahmed KM. Ki-67 expression in various diseases of gallbladder. Med J Babylon 2016;13:712-21.
19. Singh A. Ki-67 expression in premalignant and malignant lesions of gallbladder. J Med Sci Clin Res 2017;5:21528-34. doi: 10.18535/jmscr/v5i5.50.
20. Vikash, Kailashiya V, Kumar M, Puneet. EGFR expression in gallbladder carcinoma in North Indian population. Gulf J Oncolog 2023;42:47-52.
21. Agarwal A, Bansal R, Gupta M. Clinicopathological and prognostic significance of immuno-expression of Cyclin D1, E-cadherin, EGFR, HER-2, Ki67 and P53 in gall bladder cancer and its precursor lesions: a review. J Pharm Negat Results 2022;13(Suppl 9):1030-7. doi: 10.47750/pnr.2022.13.S09.123.
22. Lee CS, Pirdas A. Epidermal growth factor receptor immunoreactivity in gallbladder and extrahepatic biliary tract tumours. Pathol Res Pract 1995;191:1087-91. doi: 10.1016/S0344-0338(11)80652-7.
23. Zhou YM, Li YM, Cao N, Feng Y, Zeng F. Significance of expression of epidermal growth factor (EGF) and its receptor (EGFR) in chronic cholecystitis and gallbladder carcinoma. Ai Zheng 2003;22:262-5.
24. Sica E, Shore KT, Yang L, Phelps KC, Hammer STG, Gopal P, et al. Utility of IMP3, P53 and S100P immunohistochemical stains in

distinguishing reactive atypia from dysplasia in cholecystectomy specimens. Diagn Pathol 2024;19:129. doi: 10.1186/s13000-024-01550-w.

25. Walvir NM, Rasool Z, Masoodi S, Hassan AUL, Lone AH, Abeer I. P53 expression in gallbladder lesions: a cross-sectional study from a tertiary care centre in Northern India. J Clin Diagn Res 2024;18:10-15. doi: 10.7860/JCDR/2024/66785.18967.
26. Agarwal A, Bansal R, Gupta M. Significance of immune-markers Cyclin D1, E-cadherin, EGFR, HER-2, Ki-67 and P53 expressions in benign lesions (non-cancer diseases) of gall bladder. J Pharm Negat Results 2022;13(Suppl 9):1017-29. doi: 10.47750/pnr.2022.13.S09.122.

Author Contribution:
OAS: Planing of the study, pathological examination and writing.
ME: Planing of the study and writing.
MBB: Statistical study.