ISSN 0973-2063 (online) 0973-8894 (print)

Bioinformation 22(7): 4230-4233 (2026)

BIOINFORMATION
Discovery at the interface of physical and biological sciences

BIOMEDICAL INFORMATICS

www.bioinformation.net

Volume 22(7)

Research Article

Received July 1, 2026; Revised July 31, 2026; Accepted July 31, 2026, Published July 31, 2026

DOI: 10.6026/973206300224230

SJIF 2026 (Scientific Journal Impact Factor for 2026) = 8.478
2022 Impact Factor (2023 Clarivate Inc. release) is 1.9

Edited by Ritik Kashwani
E-mail: docritikkashwani@yahoo.com
Citation: Akter *et al.* Bioinformation 22(7): 4230-4233 (2026)

Role of immunohistochemical p53 expression as a prognostic marker in molar pregnancy

Tasrina Akter[1,*], Abu Bakar Muhammad Nizamul Hoque Sikder[2], Fahmida Sultana Mili[3], Rezowana Afrin[4], Shahana Begum[3], Roushan Akhter Jahan[3] & Shahena Akter[3]

[1]Department of Obstetrics and Gynaecology, Nottingham University Hospital, United Kingdom; [2]Department of Stroke, Nottingham University Hospital, United Kingdom; [3]Department of Obstetrics and Gynaecology, Chittagong Medical College Hospital, Chittagong, Bangladesh, India; [4]Department of Obstetrics and Gynaecology, Peterborough City Hospital, United Kingdom; *Corresponding author

Affiliation URL:
https://www.nuh.nhs.uk/
https://cmch.gov.bd/
https://www.nwangliaft.nhs.uk/peterborough-city-hospital/

ISSN 0973-2063 (online) 0973-8894 (print)
Bioinformation 22(7): 4230-4233 (2026)

Author contact:
Tasrina Akter - E-mail: tasrina.hameed@gmail.com
Abu Bakar Muhammad Nizamul Hoque Sikder - E-mail: sikder45@yahoo.com
Fahmida Sultana Mili - E-mail: sfahmida84.fsm@gmail.com
Rezowana Afrin - E-mail: rez2tanya@gmail.com
Shahana Begum - E-mail: drshahanashelly@gmail.com
Roushan Akhter Jahan - E-mail: roushanjahan2012@gmail.com
Shahena Akter - E-mail: shahena.cmc27@gmail.com

Abstract:
Malignant transformation of hydatidiform mole remains difficult to predict using conventional clinical parameters alone. A cross-sectional analytical study of 50 women showed significantly higher p53 expression in cases with elevated β-hCG levels and subsequent malignant progression. ROC analysis showed excellent predictive performance (AUC=0.938), with 87.5% sensitivity and 71.3% specificity at a 42.5% stained-cell cut-off. All patients with malignant progression showed positive p53 staining (p=0.018). Thus, data shows p53 immunoexpression as a promising prognostic biomarker for early risk stratification and clinical management of molar pregnancy.

Keywords: p53, molar pregnancy, hydatidiform mole (HM), gestational trophoblastic neoplasia (GTN), immunohistochemistry

Background:
Hydatidiform mole is the most common form of gestational trophoblastic disease characterized by abnormal proliferation of trophoblastic tissue associated with abnormal chorionic villi **[1]**. It is broadly classified into complete and partial mole according to genetic, histopathological and clinical features **[2]**. Although most molar pregnancies regress spontaneously after uterine evacuation, a significant proportion may progress to persistent gestational trophoblastic neoplasia (GTN), which can result in considerable maternal morbidity if not diagnosed and treated early **[3]**. Therefore, identification of reliable prognostic markers for predicting malignant transformation remains an important concern in clinical practice **[4]**. Serum β-human chorionic gonadotropin (βhCG) is currently considered the principal biomarker for diagnosis and follow-up of molar pregnancy **[5]**. Persistent elevation or plateau of βhCG levels after evacuation suggests progression to GTN. However, βhCG monitoring requires prolonged follow-up and repeated investigations, which may be difficult in resource-limited settings and may contribute to patient non-compliance **[6]**. Consequently, there is increasing interest in identifying tissue-based biomarkers that can predict malignant potential at an earlier stage **[7]**. Immunohistochemical detection of p53 expression has therefore gained importance as a potential prognostic indicator in several neoplastic conditions. In molar pregnancy, abnormal trophoblastic proliferation and increased cellular turnover may be associated with altered p53 expression, suggesting its possible role in predicting disease behavior and malignant transformation **[8]**. Several studies have showed increased p53 expression in trophoblastic diseases compared with normal placental tissue, with higher expression observed in cases progressing to persistent trophoblastic neoplasia **[9]**. However, the prognostic significance of p53 expression in molar pregnancy remains controversial and limited data are available from developing countries. Evaluation of p53 immunostaining may provide valuable information regarding biological aggressiveness of molar tissue and help identify patients at increased risk for progression to GTN **[10]**. Therefore, it is of interest to evaluate the role of immunohistochemical p53 expression as a prognostic marker in molar pregnancy and its association with malignant transformation.

Methodology and Materials:
This cross-sectional analytical study was conducted in the Department of Obstetrics & Gynaecology of Chittagong Medical College Hospital from 01 January 2020 to 31 December 2020. The study population comprised women with molar pregnancy admitted during the study period. Consecutive sampling technique was applied. Although the sample size was initially calculated based on sensitivity and specificity according to previous studies, due to fund and time limitations, 50 samples were finally enrolled. Patients with molar pregnancy who underwent evacuation at the hospital and provided informed consent were included. Patients with previous evacuation, negative histopathology for molar pregnancy, hemodynamic instability, unavailable pre-evacuation serum βhCG, established malignant disease, refusal to participate, or discontinuation of follow-up were excluded. After obtaining informed written consent, detailed history, physical examination and laboratory investigations including pre-evacuation serum βhCG were performed. A total of 63 samples were collected consecutively. Histopathological examination was performed after evacuation and 8 patients were excluded due to negative histopathology, while 5 were excluded because of loss to follow-up. Patients were followed for 12 weeks with serial serum βhCG measurements and categorized into gestational trophoblastic neoplasia (GTN) group or simple molar pregnancy (SMP) group according to disease progression. Immunohistochemical analysis of p53 was performed on formalin-fixed paraffin-embedded tissue sections using monoclonal mouse antibodies against p53. Nuclear staining was considered positive. The German semiquantitative scoring system was used by combining staining intensity and extent of stained cells, producing a final score ranging from 0 to 12; scores 0–3 were considered negative and 4–

12 positive. Data were analyzed using SPSS version 23. Chi-square test or Fisher's exact test was applied and ROC curve analysis was used to determine the cut-off value. A p-value <0.05 was considered statistically significant. Ethical approval was obtained from the Ethical Review Committee of Chittagong Medical College.

Results:

Table 1 presents the age distribution of the 50 study patients. The patients were categorized into three age groups. The majority of patients, 33 (66.0%), belonged to the 16–25 years age group. This was followed by 15 patients (30.0%) in the 25–40 years age group. The smallest proportion was observed in the >40 years age group, comprising only 2 patients (4.0% of the total cohort). **Table 2** presents p53 immunohistochemical expression in molar tissue from 50 patients. Regarding staining pattern, the majority showed moderate (23 cases, 46.0%) or strong (19 cases, 38.0%) staining, while weak staining was seen in only 8 cases (16.0%). Regarding extent of stained cells, the most common categories were <5% (18 cases, 36.0%) and 10–49% (18 cases, 36.0%). This was followed by 5–9% stained cells (11 cases, 22.0%). No staining (0%) was observed in 2 cases (4.0%) and only 1 case (2.0%) showed ≥50% stained cells. **Table 3** shows the association between pre-evacuation βhCG level and p53 immunostaining in 50 patients. Among 14 patients with βhCG <100,000 mIU/mL, 6 (42.9%) showed p53 positivity. Among 36 patients with βhCG >100,000 mIU/mL, 25 (69.4%) showed p53 positivity. Although the proportion of p53-positive cases was higher in the elevated βhCG group, the association was not statistically significant (p = 0.082, Fisher's exact test). **Table 4** shows the association between p53 immunostaining and disease progression (malignant transformation of hydatidiform mole) in 50 patients. All 8 patients (100%) whose disease progressed showed positive p53 immunostaining, whereas among the 42 patients whose disease regressed, 23 (54.8%) were p53-positive and 19 (45.2%) were p53-negative. The association was statistically significant (p = 0.018, Fisher's exact test). Regarding diagnostic performance, p53 immunostaining showed high sensitivity (100%) and high negative predictive value (100%), but low specificity (45.24%) and low positive predictive value (25.81%) **(Table 5)**. The overall accuracy was 54.0%. Using a ROC curve, a cut-off value of 42.5% stained cells was established to assess HM progression to gestational trophoblastic neoplasia. At this cut-off, sensitivity was 87.5% and specificity was 71.3%.

Table 1: Age distribution of the patients (n=50)

Age Group	Frequency (n)	Percentage (%)
16–25 years	33	66.0
25–40 years	15	30.0
>40 years	2	4.0
Total	50	100

Table 2: Immunohistochemical analysis of p53 in the molar tissue (n=50)

Parameter	Category	Frequency (n)	Percentage (%)
Staining pattern	Weak staining	8	16.0
	Moderate staining	23	46.0
	Strong staining	19	38.0
Extent of stained cells	0% stained cells	2	4.0
	<5% stained cells	18	36.0
	5–9% stained cells	11	22.0
	10–49% stained cells	18	36.0
	≥50% stained cells	1	2.0

Table 3: Association between pre-evacuation βhcg level and p53 immunostaining (n=50)

p53 immunostaining	pre-evacuation βhCG level		P value
	<100,000 mIU/mL (n=14)	>100,000 mIU/mL (n=36)	
Positive	6 (42.9%)	25 (69.4%)	0.082*
Negative	8 (57.1%)	11 (30.6%)	

*P value was obtained from Fisher's exact test

Table 4: Association between disease progression and p53 immunostaining (n=50)

p53 Immunostaining	Malignant Transformation of HM			P value
	Progress (n=8)	Regressed (n=42)	Total (n=50)	
Positive	8 (100.0%)	23 (54.8%)	31 (62.0%)	0.018*
Negative	0 (0%)	19 (45.2%)	19 (38.0%)	
Total	8 (16.0%)	42 (84.0%)	50 (100.0%)	

*P value was obtained from Fisher's exact test

Table 5: Diagnostic performance of p53 immunostaining for disease progression

Statistic	Value	95% CI
Sensitivity	100.00%	63.06% – 100.00%
Specificity	45.24%	29.85% – 61.33%
Positive Likelihood Ratio	1.83	1.39 – 2.40
Negative Likelihood Ratio	0	---
Disease frequency	16.00%	7.17% – 29.11%
Positive Predictive Value	25.81%	20.90% – 31.41%
Negative Predictive Value	100.00%	---
Accuracy	54.00%	39.32% – 68.19%

Discussion:

This study evaluated the role of immunohistochemical p53 expression as a prognostic marker in molar pregnancy and its association with malignant transformation. In the present study, most patients belonged to the 16–25 years age group (66.0%), while only 4.0% were older than 40 years. These findings are consistent with the epidemiological pattern of hydatidiform mole described by Buza and Hui, who reported that molar pregnancy commonly affects women in the reproductive age group, particularly in Asian populations **[10]**. In the current study, moderate and strong p53 staining patterns were observed in 46.0% and 38.0% of cases respectively, indicating increased p53 activity in trophoblastic tissue. Moreover, 36.0% of cases demonstrated staining in 10–49% of cells. These findings support the observations of Istrate-Ofițeru *et al.* who reported that abnormal trophoblastic proliferation is associated with increased immunohistochemical expression of cell-cycle regulatory proteins including p53 **[11]**. Similarly, Gupta *et al.* observed enhanced p53 expression in molar tissue with higher proliferative activity, suggesting its usefulness as a biomarker of disease aggressiveness **[12]**. The relationship between pre-evacuation serum βhCG and p53 expression was also explored in this study. Among patients with βhCG >100,000 mIU/mL, 69.4% were p53 positive compared with 42.9% positivity among patients with lower βhCG levels. Although this association did not reach statistical significance (p=0.082), the higher proportion of p53 positivity in patients with elevated βhCG suggests increased trophoblastic proliferation and malignant potential.

Comparable findings were described by Braga *et al.* who emphasized that elevated βhCG levels remain an important predictor of persistent gestational trophoblastic disease and may correlate with molecular markers associated with trophoblastic proliferation **[3]**. López *et al.* also highlighted the importance of combining histopathological and molecular biomarkers for better risk stratification in trophoblastic disease **[6]**. One of the most important findings of the present study was the significant association between p53 positivity and disease progression. All patients (100%) who developed malignant transformation showed positive p53 immunostaining, whereas only 54.8% of patients with spontaneous regression were p53 positive (p=0.018). This finding strongly suggests that increased p53 expression is associated with progression to gestational trophoblastic neoplasia. Similar observations were reported by Ren *et al.* who showed that dysregulation of tumor suppressor pathways contributes to trophoblastic neoplastic transformation **[13]**. Likewise, Badlaeva *et al.* reported that altered expression of tumor suppressor proteins including p53 is associated with aggressive biological behavior and malignant progression in neoplastic disorders **[14]**. The diagnostic performance analysis in the present study demonstrated 100% sensitivity and 100% negative predictive value of p53 immunostaining, indicating that negative p53 expression may reliably exclude malignant transformation. However, specificity (45.24%) and positive predictive value (25.81%) were relatively low, suggesting that p53 positivity alone may not be sufficient for definitive prediction. Nevertheless, ROC curve analysis revealed an excellent discriminative ability with an AUC of 0.938 (95% CI: 0.820–1.000; p<0.001). A cut-off value of 42.5% stained cells provided sensitivity of 87.5% and specificity of 71.3%, indicating good predictive accuracy. These findings are supported by Camilleri *et al.* and Szlendak *et al.* who emphasized the growing role of immunohistochemical and molecular markers in predicting tumor progression and improving risk assessment **[15, 16]**. Recent studies by Alshaikh *et al.* further showed that abnormalities in tumor suppressor signaling pathways contribute significantly to cellular invasion and metastatic potential **[17]**. Therefore, assessment of p53 expression may aid early identification of high-risk molar pregnancy patients requiring closer follow-up and timely intervention.

Conclusion:

We show the significant association between immunohistochemical p53 expression and malignant progression of molar pregnancy. Increased p53 expression showed high sensitivity and negative predictive value for predicting transformation to gestational trophoblastic neoplasia, suggesting its potential role as a useful prognostic marker. Thus, p53 immunostaining may serve as an important adjunct to serum βhCG monitoring in identifying high-risk patients who require closer surveillance and early intervention.

References:

[1] Kavyah RS *et al. Cureus.* 2025 **17**:e83716 [PMID: 40486334]
[2] Chandran JR *et al. J Obstet Gynaecol India*. 2025 **75**:365 [PMID: 40390880]
[3] Braga A *et al. Diagnostics (Basel).* 2025 **15**:1953 [PMID: 40804917]
[4] Bassyoni OY *et al. Benha Med J.* 2025 **42**:594 [DOI: 10.21608/bmfj.2025.344396.2287]
[5] Balan TA *et al. Int J Mol Sci*. 2025 **27**:142 [PMID: 41516022]
[6] López CL *et al. Clinics (Sao Paulo).* 2025 **80**:100766 [PMID: 40976132]
[7] Arafa M *et al. J Microsc Ultrastruct*. 2026 **14**:1 [PMID: 42040210]
[8] Arrillaga AO *et al. Rev Esp Patol*. 2026 **59**:100856 [PMID: 41579581]
[9] Peng M *et al. Discov Oncol*. 2025 **16**:2201 [PMID: 41258626]
[10] https://explore.openaire.eu/search/result?pid=10.1038%2Fs41379-021-00831-9
[11] Istrate-Ofițeru AM *et al. Rom J Morphol Embryol.* 2025 **66**:7 [PMID: 40384188]
[12] Gupta S *et al. Indian J Gynecol Oncolog*. 2025 **23**:19 [DOI: 10.1007/s40944-024-00953-3]
[13] Ren Y *et al. Reprod Sci*. 2026 **33**:94 [PMID: 41331236]
[14] Badlaeva A *et al. Cancers (Basel).* 2025 **17**:1398 [PMID: 40361325]
[15] Camilleri G *et al. Eur J Surg Oncol*. 2025 **51**:108727 [PMID: 39370364]
[16] Szlendak P *et al. Front Oncol*. 2026 **16**:1727634 [PMID: 42063700]
[17] Alshaikh ABA *et al. Clin Exp Metastasis*. 2026 **43**:15 [PMID: 41770291]