



A CROSS-SECTIONAL OBSERVATIONAL STUDY ON IMMUNOHISTOCHEMICAL EXPRESSION OF KI-67 AND ITS CLINICAL SIGNIFICANCE IN GESTATIONAL TROPHOBLASTIC DISEASES IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Hydatidiform moles are gestational trophoblastic lesions in which differentiation between complete and partial mole may be challenging on morphology alone. **Ki-67** is a nuclear marker of cellular proliferation and may provide an adjunctive assessment of trophoblastic proliferative activity. **Objective:** To study the pattern of Ki-67 expression in hydatidiform moles and correlate its expression with clinicopathological parameters. **Methods:** This cross-sectional observational study included 50 histopathologically proven hydatidiform moles from Modern Government Maternity Hospital, Petlaburj, Hyderabad, collected over two years. Representative formalin-fixed, paraffin-embedded tissue sections were evaluated by H&E staining and Ki-67 immunohistochemistry. Ki-67 staining was graded as 0, 1+, 2+, or 3+ according to the study scoring system. **Results:** Of 50 cases, 37 (74%) were complete moles and 13 (26%) were partial moles. Patient age ranged from 18–35 years, with a mean age of 24 years. Complete moles showed predominantly strong Ki-67 expression: 23/37 (62%) were 3+ and 14/37 (38%) were 2+. Among partial moles, 1/13 (8%) was negative, 7/13 (54%) showed 1+ staining, and 5/13 (38%) showed 2+ staining; no partial mole showed 3+ staining. Overall, 42/50 (84%) cases showed strong staining, 7/50 (14%) weak staining and 1/50 (2%) negative staining. **Conclusion:** Ki-67 showed stronger nuclear expression in complete than partial hydatidiform moles and may be a useful adjunct to routine H&E examination for their differentiation. Cases with overlapping staining require correlation with morphology and, where indicated, additional ancillary techniques.

KEYWORDS : Gestational Trophoblastic Disease; Hydatidiform Mole; Complete Mole; Partial Mole; Ki-67; Immunohistochemistry; Trophoblast.

INTRODUCTION

Gestational trophoblastic diseases (GTDs) comprise proliferative disorders of placental trophoblast and include hydatidiform moles and gestational trophoblastic neoplasms. Hydatidiform moles are classified into complete and partial moles, with invasive mole representing a form of molar gestation with myometrial or vascular invasion.

Distinguishing complete hydatidiform mole (CHM) from partial hydatidiform mole (PHM) is clinically important because their risks of progression to gestational trophoblastic neoplasia differ. Histopathological assessment may show considerable intraobserver and interobserver variability, prompting the use of ancillary methods such as ploidy analysis, short-tandem-repeat genotyping, FISH and p57 immunohistochemistry.

Ki-67 is a nuclear proliferation marker expressed during active phases of the cell cycle (G1, S, G2 and mitosis) and absent in resting cells. Its expression can therefore reflect trophoblastic proliferative activity and may assist in differentiating molar lesions. The study was designed to evaluate Ki-67 expression and its clinicopathological significance in hydatidiform moles.

AIMS AND OBJECTIVES

1. To study the pattern of expression of Ki-67 in gestational trophoblastic disease.
2. To correlate Ki-67 expression with clinicopathological parameters.
3. To study and grade the severity of gestational trophoblastic disease based on the Ki-67 staining pattern.

MATERIALS AND METHODS

Study Design and Setting: Cross-sectional observational study conducted over a period of two years at Modern Government Maternity Hospital, Petlaburj, Hyderabad.

Study Population and Sample Size: A convenient sample of 50 clinically diagnosed gestational trophoblastic disease cases was included. The final study cohort comprised histopathologically proven hydatidiform moles: 37 complete moles and 13 partial moles.

Inclusion Criteria: Patients who provided informed consent and had newly diagnosed gestational trophoblastic disease.

Exclusion Criteria: Refusal of consent, inadequate biopsy material for immunohistochemistry, and patients who had received chemotherapy before uterine evacuation.

Histopathology and Immunohistochemistry: A representative formalin-fixed, paraffin-embedded tissue block from each case was sectioned. H&E-stained sections were evaluated for histopathological diagnosis. Separate sections were subjected to Ki-67 immunohistochemistry with appropriate positive and negative controls. Ki-67 was interpreted as a nuclear stain; cytoplasmic staining was disregarded.

Ki-67 Scoring: The study categorized staining into 0, 1+, 2+ and 3+ grades. For the overall summary, negative corresponded to 0, weak to 1+, and strong staining to the higher grades as reported in the dissertation.

RESULTS

Fifty cases of hydatidiform mole were studied. Complete mole accounted for 37 cases (74%), while partial mole accounted for 13 cases (26%). The age range was 18–35 years, with a mean age of 24 years. The largest age group was 22–25 years (21/50; 42%).

Complete moles were more frequent in the 22–25-year age group, whereas partial moles were more frequent in the 26–29-year age group. Both entities were more common in the second trimester; complete moles predominated before 16 weeks, while partial moles predominated at 17–25 weeks. The reported association between histopathological diagnosis and gestational age was statistically significant (Pearson chi-square = 27.261; $p = 0.007$).

Serum b-hCG levels were higher in complete moles, with >100,000 mIU/mL reported in 32/37 complete moles and 9/13 partial moles. Overlap in b-hCG values between the groups was also noted.

Ki-67 expression showed a clear difference in distribution between the two histopathological groups. All 37 complete moles were positive at 2+ or 3+: 14 (38%) showed 2+ staining and 23 (62%) showed 3+ staining. Among

the 13 partial moles, 1 (8%) was negative, 7 (54%) showed 1+ staining and 5 (38%) showed 2+ staining; none showed 3+ staining.

Across all 50 cases, 1 (2%) was negative, 7 (14%) showed weak staining and 42 (84%) showed strong staining.

DISCUSSION

The principal finding of this study is the higher intensity of Ki-67 nuclear staining in complete hydatidiform moles compared with partial moles. This supports the concept that Ki-67 reflects the increased proliferative activity of trophoblastic cells in complete mole.

The findings are consistent with the cited literature summarized in the dissertation. Previous studies reported lower Ki-67 indices in partial moles than complete moles and suggested that Ki-67 can assist in differentiating these entities. A meta-analysis cited in the dissertation reported Ki-67 positivity in 163/188 complete moles and 103/149 partial moles, with an odds ratio of 3.28, supporting the potential value of Ki-67 as an adjunctive marker.

However, Ki-67 should not be interpreted in isolation. In the present study, five partial moles showed 2+ staining, creating an overlap zone with complete moles. Correlation with routine H&E morphology and use of additional ancillary techniques in difficult cases remain important.

The clinical relevance lies in improving diagnostic confidence in a setting where accurate classification influences follow-up and risk assessment. The stronger Ki-67 expression observed in complete moles is also biologically relevant given their higher reported risk of progression to gestational trophoblastic neoplasia.

Limitations

The sample size was limited to 50 cases and was selected by convenience sampling. The study was performed at a single tertiary-care center. It primarily evaluated histopathologically proven complete and partial moles and therefore does not establish the performance of Ki-67 across the entire spectrum of GTD.

The dissertation reports intensity categories rather than a universally standardized Ki-67 labeling-index threshold. Therefore, the findings are best interpreted as an adjunctive semiquantitative observation rather than as a validated diagnostic cut-off.

CONCLUSION

Ki-67 immunohistochemistry demonstrated stronger nuclear expression in complete hydatidiform moles than in partial hydatidiform moles in this cross-sectional series. When combined with routine H&E examination, Ki-67 may serve as a useful adjunct for differentiating complete and partial molar pregnancies. Because some partial moles showed moderate staining and therefore overlapped with complete moles, Ki-67 should be interpreted with morphology and, in diagnostically difficult cases, complementary ancillary investigations.

Key Results Table

Ki-67 grade	Complete mole n (%)	Partial mole n (%)	Total n (%)
0 (negative)	0 (0)	1 (8)	1 (2)
1+ (weak)	0 (0)	7 (54)	7 (14)
2+ (moderate)	14 (38)	5 (38)	19 (38)
3+ (high)	23 (62)	0 (0)	23 (46)
Total	37 (100)	13 (100)	50 (100)

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