Barind Medical College Journal
Abbreviated Key Title: BMCJ
ISSN: 2518-3249 (Print)
https://bmcj.org/index.php/bmcj
Volume-10 | Issue-2 | July-Dec, 2024 | DOI: https://doi.org/10.70818/bmcj.2024.v010i02.012

OPEN ACCESS

Original Research Article

Influence of Socio-demographic Factors and the Expression of Ki-67 Immunohistochemical Marker in Hydatidiform Mole Development

Dr. Sonia Hossain[a]*, Dr. Farjana Pervin Nupur[b], Dr. Munira Anjum[c], Dr. Md. Nazmus Sakib[d], Dr. Mehnaj Nasrin[e]

[a]Department of Pathology, Dhaka Medical College, Dhaka, Bangladesh
[b]Lecturer, Department of Pathology, Dhaka Medical College, Dhaka
[c]Assistant professor Department of pathology Marks Medical College, Dhaka
[d]Junior Consultant (Surgery), UHC, Atpara, Netrakona
[e]Medical Officer, Pathology Mugda Medical College

***Correspondence to:**
Dr. Sonia Hossain
Department of Pathology, Dhaka Medical College, Dhaka, Bangladesh
Email:sondhisoniahossain69@gmail.com

Article History
Received: 14.10.2024
Accepted: 11.11.2024
Published: 31.12.2024

Abstract: ***Background*:** Hydatidiform mole is a significant concern in obstetric care, affecting approximately 1 in every 1000 pregnancies globally. Unfortunately, Asians demonstrate slightly higher incidence rates compared to Europeans of similar socioeconomic status. ***Objective:*** This study aimed to find out the associations between sociodemographic factors and expression of Ki-67 immunohistochemical marker with hydatidiform mole. ***Methods:*** In this cross-sectional observational study, conducted at the Department of Pathology, Dhaka Medical College, 50 cases were classified into Complete Hydatidiform Mole (CHM) and Partial Hydatidiform Mole (PHM) based on histopathological features. Pretreatment β-hCG levels were noted, and Ki-67 immunohistochemistry was performed. The results of the cases were collected and tabulated. Statistical analysis was conducted on the tabulated data using Fisher's exact test, chi-square test. ***Results:*** Among the respondent's majority 40% (20) had age ≤ 20 years and only 8% (4) had age more than 40 years. This association between parity of respondents with Ki-67 immunoexpression was statistically significant ($p<0.05$). Primigravida patients were more likely to have a Ki-67 score of 2 and multigravida patients more likely to have a Ki-67 score of 3. Moreover, parity and Ki-67 immunoexpression scoring of the respondents were significantly associated with hydatidiform mole diagnosis after immunohistochemical evaluation ($p<0.05$) and ($p<0.01$) respectively. ***Conclusion:*** The results indicate that certain sociodemographic variables do not have a substantial impact on the type of hydatidiform mole, whereas reproductive factor (parity) and levels of Ki-67 expression play vital role.

Keywords: Hydatidiform Mole In, Complete Hydatidifrom Mole, Partial Hydatidiform Mole, Socio-Demographic Factors, Ki- 67 Immunomarker.

Cite this as: Hossain S, Nupur FP, Anjum M, Sakib MN, Nasrin M. Influence of Socio-demographic Factors and the Expression of Ki-67 Immunohistochemical Marker in Hydatidiform Mole Development. BMCJ. 2024;10(2):16-22.

Introduction

Hydatidiform mole (HM), sometimes referred to as molar pregnancy, is a rare abnormality characterized by trophoblastic tissue proliferating abnormally, resulting in the development of a grape-shaped cyst inside the uterine cavity.[1] The possibility of malignant development into gestational trophoblastic neoplasia (GTN) is one of the major medical challenges associated with this condition for women.[2] Hydatidiform lesions can be classified as either complete or partial. While

some foetal parts may be visible in a partial mole but complete moles do not.[3] In general, complete moles are diploid, while partial moles are triploid.[4] Understanding the divert sociodemographic risk factors as well as possible immunohistochemistry markers like Ki-67 expression can be extremely helpful in diagnosing, treating, and preventing the condition.

Hydatidiform mole is a significant concern in obstetric care, affecting approximately 1 in every 1000 pregnancies globally.[5] Unfortunately, Asians demonstrate slightly higher incidence rates compared to Europeans of similar socioeconomic status.[6] In Bangladesh, although comprehensive epidemiological data on HM are limited but its occurrence is not uncommon. An earlier study conducted in Rajshahi Medical College Hospital reported that between 2016-2017 incidence of molar pregnancy was 5.3 per 1,000 deliveries that was 1 in 188 deliveries.[7] Another study carried out in Rangpur district reported 11 (2.1%) patients were diagnosed as hydatidiform mole among 519 pregnant women.[8] Reducing the burden of HM is critical to improving maternal health outcomes because of our sociocultural background, where remote areas may have inadequate access to healthcare facilities and knowledge about reproductive health.

A wide range of maternal risk factors and sociodemographic characteristics are associated with hydatidiform moles (HM). Consistently, advanced maternal age has been identified as a risk factor for HM, specifically in women who are 35 years or older.[9] Furthermore, nulliparity and a history of prior molar pregnancies are important risk factors for HM development.[10] Additionally, socioeconomic status, ethnic origin, and geographic location are significant factors, as evidenced by the observed disparities in HM incidence among populations.[11] Due to inadequate prenatal care and barriers to healthcare access, women from low-inome households may be at a greater risk. Toxic environmental exposures, obesity, smoking, and other lifestyle choices raise the risk of heavy metal poisoning.[10-12]

On the other hand, Ki-67, a nuclear protein associated with cellular proliferation, is frequently used as an immunohistochemical marker.[13] Elevated levels of Ki-67 expression have been associated with a higher chance of malignant transformation.[14] Conducting a study on hydatidiform mole in Bangladesh is crucial due to limited data on its prevalence and impact in the country. Limited healthcare access and lack of health education in rural areas may contribute to delayed diagnosis and adverse maternal outcomes in hydatidiform mole. Understanding sociodemographic factors associated with hydatidiform mole can help identify vulnerable populations and guide targeted interventions to improve maternal health. Additionally, exploring the expression of Ki-67 as an immunohistochemical marker may thereby potentially facilitate the development of effective risk stratification methods.

Methods

It was a large part of a cross sectional study. This research was carried out at the Department of Pathology, Dhaka Medical College, spanning from March 2021 to February 2023. A total of 50 cases were included in the study, selected through non-probability purposive sampling. Detailed relevant information and demographic data, along with pretreatment β-hCG values, were meticulously gathered from the patients. Hematoxylin & Eosin (H&E) stained sections were carefully examined to assess morphological features. The cases were categorized into Complete Hydatidiform Mole (CHM) and Partial Hydatidiform Mole (PHM) based on specific histopathological criteria. Additionally, an immunohistochemical stain using Ki-67 was carried out. Evaluation of immunostaining was performed by light microscopy. Primary antibody was -Monoclonal Mouse Anti-Human Ki 67 antigen Clone MIB-1 Ready to use (LINK). Secondary Antibody was DAKO REALTM EnVision TM (HRP RABBIT/MOUSE) (ENV). Positive control was Normal lymphocytes in the lymphoid follicle of an appendix. Brownish nuclear staining of proliferating trophoblastic cells was considered Ki 67 scoring. Notably, the thesis protocol received approval from the Ethical Review Committee of Dhaka Medical College, Dhaka. Statistical analysis was done by SPSS (version 21) and statistical significance was set at $p<0.05$.

Results

This cross-sectional study was conveyed among 50 patients of histologically diagnosed complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM). Immunohistochemical expression of Ki 67 was observed among them. The results and observations are given below.

Table 1: Distribution of socio-demographic characteristics of the respondents (n=50)

Attributes		Frequency (f)	Percent (%)
Age (Years)	≤ 20	20	40
	21- 30	19	38
	31-40	7	14
	> 40	4	8
Gestational age	< 12 weeks	17	34
	12-16 weeks	33	66
Parity	Primigravida	19	38
	Multigravida	31	62
Blood group	A (+) ve	20	40
	B (+) ve	17	34
	B (-) ve	2	4
	AB (+) ve	2	4
	O (+) ve	8	16
	O (-) ve	1	2

Among the respondents majority 40% had age ≤ 20 years (n=20) and only 8% had age more than 40 years (n=4). Gestational age was within 12-16 weeks among majority 66% of respondents (n=33) and 62% of respondents were multigravida (n=31). Regarding blood group majority 40% of respondents belonged to A positive (n= 20) and only 2% belonged to O negative (n=1) presented in (Table-1).

Table 2: Distribution of respondents by pathological findings

Attributes		Frequency (f)	Percent (%)
β HCG level	≤100000	24	48
	>100000	26	52
Histopathological type	CHM	27	54
	PHM	23	46
Ki-67 immunoexpression scoring	Score-2	26	52
	Score-3	24	48
Diagnosis after evaluation	CHM	24	48
	PHM	26	52

Table-2 stated that majority 52% of respondents (n=26) had β HCG level more than 1,00,000. Histopathologically 54% of respondents (n=27) were diagnosed as complete hydatidiform mole and the rest 46% were (n=23) diagnosed as partial hydatidiform mole cases. Ki-67 immunoexpression was score-2 among 52% of respondents (n=26) and the rest 48% had score-3 (n=24). After immunohistochemical evaluation 52% of respondents (n=26) were diagnosed as CHM and 48% respondents (n=24) were diagnosed as PHM.

Table 3: Association between different characteristics of respondents with histopathological diagnosis of hydatidiform mole (n=50)

Clinical features	Histopathological diagnosis		Significance
	CHM (n =27) f (%)	PHM (n =23) f (%)	
Age (Years)			
≤20	12 (60)	8 (40)	p =0.918
21-30	10 (52.6)	9 (47.4)	
31-40	3 (42.9)	4 (57.1)	
≥40	2 (50)	2 (50)	
Gestational age (Weeks)			
≤12	9 (52.9)	8 (47.1)	p =0.914
12-16	18 (54.5)	15 (45.5)	
Blood group			
A (+ve)	12 (60)	8 (40)	p =0.183
B (+ve)	11 (64.7)	6 (35.3)	
B (-ve)	0 (0)	2 (100)	
AB (+ve)	1 (50)	1 (50)	
O (+ve)	2 (25)	6 (75)	
O (-ve)	1 (100)	0 (0)	
Parity			
Primigravida	8 (42.1)	11 (57.9)	p =0.186
Multigravida	19 (61.3)	12 (38.7)	

Table-3 shows age, gestational age, blood group, parity of respondents were not significantly associated with histopathological diagnosis of hydatidiform mole.

Table 4: Association between different characteristics of respondents with Ki-67 immunoexpression (n=50)

Clinical features	Ki-67 immunoexpression		Significance
	Score-2 f (%)	Score-3 f (%)	
Age (Years)			
≤20	11 (55)	9 (45)	p =0.971
21-30	9 (47.4)	10 (52.6)	
31-40	4 (57.1)	3 (42.9)	
≥40	2 (50)	2 (50)	
Gestational age (Weeks)			
≤12	8 (47.1)	9 (52.9)	p =0.616
12-16	18 (54.5)	15 (45.5)	
Blood group			
A (+ve)	9 (45)	11 (55)	p =0.214
B (+ve)	9 (52.9)	8 (47.1)	
B (-ve)	2 (100)	0 (0)	
AB (+ve)	0 (0)	2 (100)	
O (+ve)	6 (75)	2 (25)	
O (-ve)	0 (0)	1 (100)	
Parity			
Primigravida	14 (73.7)	5 (26.3)	p =0.016*
Multigravida	12 (38.7)	19 (61.3)	

Table-4 represents that age, gestational age and blood group of respondents were not significantly associated with Ki-67 immunoexpression. Among the respondents who were primigravida, 73.7% belonged to score-2 Ki-67 immunoexpression (n=14) and who were multigravida 61.3% belonged to score-3 Ki-67 immunoexpression (n=19). This differences of parity of respondents with Ki-67 immunoexpression was statistically significant (p<0.05).

Table 5: Association between different characteristics of respondents with immunohistochemical diagnosis of hydatidiform mole after evaluation (n=50)

Clinical features	IHC diagnosis after evaluation		Significance
	CHM (n =24) f (%)	PHM (n=26) f (%)	
Age (Years)			
≤20	8 (40)	12 (60)	p =0.740
21-30	11 (57.9)	8 (42.1)	
31-40	3 (42.9)	1 (57.1)	
≥40	2 (50)	2 (50)	
Gestational age (Weeks)			
≤12	9 (52.9)	8 (47.1)	p =0.616
12-16	15 (45.5)	18 (54.5)	
Blood group			
A (+ve)	11 (55)	9 (45)	p =0.355
B (+ve)	7 (41.2)	10 (58.8)	
B (-ve)	1 (50)	1 (50)	
AB (+ve)	2 (100)	0 (0)	
O (+ve)	2 (25)	6 (75)	
O (-ve)	1 (100)	0 (0)	
Parity			
Primigravida	5 (26.3)	14 (73.7)	p =0.016
Multigravida	19 (61.3)	12 (38.7)	

Table-5 showed that parity of the respondents were significantly associated with hydatidiform mole diagnosis after immunohistochemical evaluation (p<0.05).

Table 6: Association between Ki-67 immunoexpression scoring with diagnosis of hydatidiform mole after immunohistochemical evaluation (n=50)

Ki-67 immunoexpression	Diagnosis after IHC evaluation		Significance
	CHM (n=24) f (%)	PHM (n=26) f (%)	
Score-2	1 (3.8)	25 (96.2)	p = 0.000*
Score-3	23 (95.8)	1 (4.2)	

Ki-67 immunoexpression scoring was found significantly associated with diagnosis of hydatidiform mole after immunohistochemical evaluation (p<0.01).

Discussion

The study aimed to explore the association between sociodemographic characteristics with hydatidiform mole and the expression of the Ki-67 immunohistochemical marker among a sample of 50 patients. The findings of this study provided valuable insight of the patients' sociodemographic attributes, pathological findings, and the relationship of these factors with the Ki-67

expression and the histopathological diagnosis of hydatidiform mole. Firstly, the higher incidence in younger women (≤20 years) might be associated with hormonal and reproductive factors prevalent in this age group, such as higher levels of human chorionic gonadotropin (hCG) which can influence trophoblastic proliferation. The higher chance of hydatidiform mole in younger women consistent with previous studies that suggest age as a risk factor for molar pregnancies.[15] Additionally, the predominance of multigravida patients (62%) could indicate that repeated pregnancies and associated hormonal changes may increase susceptibility to molar pregnancies. Earlier studies also explored repeated pregnancies as a major concern of molar pregnancies.[16] Gestational age at diagnosis was predominantly within 12-16 weeks (66%), and a majority of the patients were multigravida (62%). Blood group distribution showed that 40% of the patients had A positive blood type, which is consistent with some literature suggesting a possible association between certain blood groups and the risk of molar pregnancy. Compared to other blood group group A and AB had an elevated relative risk (RR) of molar pregnancy (RR = 1.4 and 2.3 respectively).[17] These demographic factors warrant further researches to understand the underlying mechanisms and potential genetic or immunological predispositions that contribute to the development of hydatidiform moles.

Our study revealed that 52% of the patients had β HCG levels exceeding 100,000 mIU/mL, reflecting the aggressive trophoblastic proliferation typical of hydatidiform moles. Histopathological evaluation diagnosed 54% of the cases as complete hydatidiform mole (CHM) and 46% as partial hydatidiform mole (PHM). This finding is discordant with the previous studies with higher prevalence of PHM over CHM.[16] The Ki-67 immunoexpression, which serves as a marker for cellular proliferation, was scored as 2 in 52% of the cases and 3 in 48%. This indicates a high proliferative index in a significant number of patients, correlating with the aggressive nature of molar pregnancies. When evaluating the association between sociodemographic characteristics and histopathological diagnosis, the study found no significant association with age, gestational age, blood group, or parity ($p > 0.05$). This suggests that these sociodemographic factors alone may not significantly influence whether a patient is diagnosed with CHM or PHM. This finding aligns with some studies but contrasts with others that have found certain sociodemographic factors to be influential, indicating the need for further research to clarify these relationships.[4]

However, parity showed a significant association ($p < 0.016$), with primigravida patients more likely to have a Ki-67 score of 2 and multigravida patients more likely to have a Ki-67 score of 3. This suggests that the proliferative activity as indicated by Ki-67 expression might be influenced by the number of previous pregnancies. The study's immunohistochemical evaluation post-Ki-67 scoring indicated that parity was significantly associated with the final diagnosis of hydatidiform mole ($p = 0.016$). Specifically, primigravida patients were more likely to be diagnosed with PHM, while multigravida patients were more likely to be diagnosed with CHM. This association underscores the potential impact of reproductive history on the type of molar pregnancy. Additionally, Ki-67 immunoexpression was significantly associated with the final diagnosis after immunohistochemical evaluation ($p < 0.01$). Specifically, a Ki-67 score of 2 was predominantly associated with PHM, while a score of 3 was predominantly associated with CHM. This strong association highlights the utility of Ki-67 as a marker for differentiating between CHM and PHM, providing valuable diagnostic information that can guide clinical management.[18]

Conclusion

The study highlights the association between sociodemographic characteristics and the pathological features of hydatidiform mole, with specific emphasis on the Ki-67 immunohistochemical marker. The findings suggest that while some sociodemographic factors do not significantly influence the type of hydatidiform mole but reproductive history (parity) and Ki-67 expression levels are critical factors. These insights can enhance the understanding and management of hydatidiform mole, promoting better patient outcomes through tailored diagnostic and therapeutic strategies.

Declarations

Ethics approval and consent to participate

Before data collection, both verbal and written informed consent was taken from patients.

Consent for publication

All authors have approved this manuscript for publication.

Availability of data and materials

The datasets supporting the conclusions of this article are included within the article generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

SH, FPN, MA participated in the design of the study, data interpretation and drafted the manuscript. SH, NS, MN contributed to the data design, data interpretation and data analysis with critical review. All authors read and approved the final manuscript.

Acknowledgements

We are grateful to all the patients gave information for the study.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no funding.

References

1. Savage P, Williams J. Article in The Journal of reproductive medicine. 2009. Available from: https://www.researchgate.net/publication/46007622
2. Soper JT. Gestational Trophoblastic Disease: Current Evaluation and Management. Obstetrics and Gynecology. 2021 Feb 1;137(2):355–70.
3. Candelier JJ. The hydatidiform mole. Vol. 10, Cell Adhesion and Migration. Taylor and Francis Inc.; 2016. p. 226–35.
4. Mulisya O, Roberts DJ, Sengupta ES, Agaba E, Laffita D, Tobias T, et al. Prevalence and Factors Associated with Hydatidiform Mole among Patients Undergoing Uterine Evacuation at Mbarara Regional Referral Hospital. Obstet Gynecol Int. 2018;2018.
5. Florea A, Caba L, Grigore AM, Antoci LM, Grigore M, Gramescu MI, et al. Hydatidiform
6. Mole—Between Chromosomal Abnormality, Uniparental Disomy and Monogenic Variants: A Narrative Review. Life. 2023 Dec 10;13(12):2314.
7. Tham B. Gestational trophoblastic disease in the Asian population of Northern England and North Wales. BJOG. 2003 Jun;110(6):555–9.
8. Nargis Shamima M, Zereen R, Alamgir Hossain M, Zahan N, Akter N, Rawson Ara Khatun M. Evaluation of molar pregnancy in Rajshahi Medical College Hospital. Vol. 9, KYAMC Journal. 2018.
9. Taher MA. Incidence of gestational trophoblastic disease in Rangpur, Bangladesh Bangladesh Atomic Energy Commission, Nuclear Medicine Centre, Rangpur, Bangladesh HE ASEAN JOURNAL OF RADIOLOGY. SEPT. - DEC. 2003 Volume LX Number III doi:10.1016/S0301-5629(03)00510-6 (umbjournal.org)
10. Savage PM, Sita-Lumsden A, Dickson S, Iyer R, Everard J, Coleman R, et al. The relationship of maternal age to molar pregnancy incidence, risks for chemotherapy and subsequent pregnancy outcome. J Obstet Gynaecol (Lahore). 2013 May;33(4):406–11.
11. Al-Talib AA. Clinical presentation and treatment outcome of molar pregnancy: Ten years experience at a Tertiary Care Hospital in Dammam, Saudi Arabia. J Family Community Med. 2016 Sep 1;23(3):161–5.
12. Milani HS, Abdollahi M, Torbati S, Asbaghi T, Azargashb E. Risk factors for hydatidiform mole: Is Husband's job a major risk factor? Asian Pacific Journal of Cancer Prevention. 2017 Oct 1;18(10):2657–62.
13. Niloufar A, Hamideh P, Monirsadat M, Ali E, Farahani Ahmadreza V. Molar Pregnancy and Its Associated Risk Factors: A Case-Control Study in Qazvin, Iran. Journal of Advanced Biomedical Sciences | Winter. 2021;11. Available from: https://doi.org/10.18502/jabs.
14. Nyein Soe N, Wut Hmone S, Myint Nyein M, Mon M. 67 Immunoexpression in Gestational Trophoblastic Diseases. Vol. 30, Myanmar Health Sciences Research Journal. 2018.
15. Semary SEDS, Abd-Elrahman ASA, Mohammed MH. The Utility of P53, P63, P57 and Ki67 Immunohistochemistry in the

Differentiation between Hydropic Abortion and Molar Pregnancy (Immunohistochemical Study). Vol. 73, The Egyptian Journal of Hospital Medicine. 2018.

16. Tumours of the placenta. Available from: http://oncology.thelancet.com
17. Joyce CM, Fitzgerald B, McCarthy T V, Coulter J, O'Donoghue K. Advances in the diagnosis and early management of gestational trophoblastic disease. BMJ Medicine [Internet]. 2022 Dec;1(1):e000321. Available from: https://bmjmedicine.bmj.com/lookup/doi/10.1136/bmjmed-2022-000321
18. Parazzini F, Vecchia C La, Franceschi S, Pampallona S, Decarli A, Mangili G, et al. ABO BLOOD-GROUPS AND THE RISK OF GESTATIONAL TROPHOBLASTIC DISEASE. Vol. 71, Tumori. 1985.
19. Hasanzadeh M, Sharifi N, Esmaieli H, Daloee MS, Tabari A. Immunohistochemical expression of the proliferative marker Ki67 in hydatidiform moles and its diagnostic value in the progression to gestational trophoblastic neoplasia. Journal of Obstetrics and Gynaecology Research. 2013 Feb;39(2):572–7.