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Multivariate Analysis of Risk Factors for Persistent Gestational Trophoblastic Neoplasia in Patients with Hydatidiform Mole

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Abstract

Introduction: Gestational trophoblastic disease (GTD) is a group of neoplastic disorders that arise from placental trophoblast cells following abnormal fertilization. Persistent Gestational Trophoblastic Neoplasia (PGTN) is a severe complication that can occur following a hydatidiform mole, requiring the early identification of high-risk patients. This study aimed to analyze the risk factors associated with PGTN in patients with hydatidiform moles using multivariate analysis.

Methods: A retrospective analysis was conducted on 50 patients diagnosed with hydatidiform moles, categorized into GTN-positive (n=7) and GTN-negative (n=43) groups at the Gynecological Oncology Outpatient Department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2021 to December 2021.

Result: Age and BMI were significantly associated with GTN positivity (p=0.024 and p=0.012, respectively). GTN-positive patients were predominantly under 20 years old (71.4%) and underweight (100%). A history of abortion was absent in all GTN-positive cases, while the presence of grape-like vesicles (100%), larger vesicle size (>2 cm), and a history of molar pregnancy (71.4%) were significantly more common in the GTN-positive group ($p<0.05$). Ultrasound findings showed a higher prevalence of cystic vesicles and theca lutein cysts >6 cm in GTN-positive patients ($p<0.05$). Initial post-evacuation β-hCG levels were significantly higher in GTN-positive cases ($p<0.05$), with levels in weeks 5 to 8 demonstrating the strongest predictive power for GTN development (AUC = 99.7%). Multivariate analysis identified younger age as a significant independent risk factor for PGTN (OR: 1.17, 95% CI: 1.02–16.3, $p<0.05$), while the history of molar pregnancy, thyrotoxic features, and uterine size were not significantly associated.

Conclusion: The findings show that younger age, low BMI, larger vesicle size, high initial β-hCG levels, and prolonged elevated β-hCG levels (weeks 5–8) were significant predictors of GTN development. History of a mole in a previous pregnancy, thyrotoxic features, and uterine size per abdomen were also risk factors but were not significantly associated with PGTN. Close monitoring of these risk factors can aid in the early identification and management of high-risk patients to prevent progression to PGTN.

Keywords: Multivariate Analysis, Risk Factors, Persistent Gestational Trophoblastic Neoplasia, Hydatidiform Mole

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Introduction

Gestational trophoblastic disease (GTD) is a group of neoplastic disorders arising from placental trophoblast cells after abnormal fertilization. According to the WHO classification, GTD includes both benign and malignant forms [1]. The benign form, known as a hydatidiform mole, can be either complete or partial. The malignant forms, collectively termed gestational trophoblastic neoplasia (GTN), include invasive moles, choriocarcinoma, placental site trophoblastic tumors (PSTT), and epithelioid trophoblastic tumors. These conditions vary in severity, but all originate from the trophoblastic tissue of the placenta [2]. The incidence of GTD varies in different parts of the world, for example, in Japan, the incidence is 2/1000 deliveries while in Malaysia, the incidence of molar pregnancy and gestational trophoblastic neoplasia is 2.8/1000 and 1.59/1000 deliveries respectively [2,3]. Meanwhile, in North America, its incidence is reported up to 2.5/1000 pregnancies [4]. The highest incidence of 12.1/1000 deliveries is reported from Turkey [5]. The malignant potential of this disease is higher in South East Asia where it is as high as 10– 15% compared to 2–4% in Western countries [6].

Molar pregnancy is now classified as either complete or partial based on its gross appearance, microscopic histopathology, and karyotypic characteristics. Early detection of persistent gestational trophoblastic tumor (GTT) relies on careful monitoring of post-molar β-hCG levels and maintaining a high index of suspicion in women of reproductive age who present with unexplained gynecologic or systemic symptoms [3]. Studies suggest that earlier diagnosis of a complete mole is associated with more subtle pathological features compared to cases identified later in pregnancy. While most molar pregnancies occur sporadically, a familial syndrome of recurrent hydatidiform moles has been documented [4]. Persistent Gestational Trophoblastic Neoplasia (PGTN) is a complex subset of GTN that requires prolonged follow-up and individualized treatment. Among malignant forms, choriocarcinoma is particularly aggressive, with an incidence of approximately 1 in 40,000–50,000 pregnancies and occurring in about 1 in 40 cases of hydatidiform mole [7,8]. Post-molar GTN is diagnosed based on rising β-hCG levels and imaging findings suggestive of persistent molar tissue. Histological confirmation is typically unnecessary unless a placental site trophoblastic tumor (PSTT) is suspected. Post-molar GTN is defined by specific criteria, including a plateau in β-hCG levels (four values within ±10%) over three weeks (days 1, 7, 14, 21), a rise in β-hCG levels by more than 10% across three measurements over two weeks (days 1, 7, 14), persistent detectable β-hCG for more than six months after molar evacuation, histopathological confirmation of choriocarcinoma and evidence of metastatic disease [9].

The risk factors for malignant disease were studied and WHO proposed a scoring system which was adopted by FIGO in stratifying patients into high-risk and low-risk categories for propensity to progress to malignancy. Extremes of age are known risk factors for GTN. Women with pre-evacuation beta-hCG of more than 1 lakh, excessive uterine enlargement, and theca lutein cysts more than 6 cm diameter are particularly at high risk. The major well-established risk factors for the disease are advanced maternal age and a history of GTD [10]. According to Mousavi et al, the rate of decrease in beta-hCG level at two weeks post-evacuation is the most reliable and strongest predictive factor for the progression of molar pregnancies to neoplasia [11]. Several studies have attempted to identify factors that would predict persistent GTN or remission to better inform patients and their physicians regarding the risk of developing persistent GTN [12,13]. Other studies have discussed the possibility of identifying persistent GTN based on the level of beta-hCG at a given time point post evacuation and patients who go on to have persistent GTN have beta-hCG regression patterns that differ from patients who go on to remission [11,14,15]. Since this group of disorders is now one of the highly curable neoplasms, early diagnosis and prompt treatment are necessary. Therefore, in this study, we aimed to analyze the risk factors associated with PGTN in patients with hydatidiform moles using multivariate analysis.

Methodology and Materials

This cross-sectional study was conducted at the Gynecological Oncology Outpatient Department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2021 to December 2021. We included 50 participants diagnosed with molar pregnancy based on histopathological confirmation. These are the following criteria to be eligible for enrollment as our study participants: a) Patients aged above 18 years old; b) Patients with a histopathologically confirmed diagnosis of molar pregnancy; c) Patients who were willing to participate were included in the study And a) Patients with diagnosed abortions, such as missed or incomplete abortions; b) Patients with a prior hysterectomy performed due to molar pregnancy; c) Patients with any history of acute illness (e.g., renal or pancreatic diseases, ischemic heart disease, asthma, COPD, etc.) or infection were excluded from our study.

Data Collection

Persistent gestational trophoblastic neoplasia (PGTN) was identified as the persistence of gestational trophoblastic disease (GTD) indicated by elevated levels of beta human chorionic gonadotropin (β-hCG). All participants provided informed written consent, ensuring their voluntary participation and maintaining confidentiality. Detailed clinical evaluations and histories were obtained, and ultrasonography

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along with serum β-hCG levels confirmed the diagnosis of molar pregnancy. Following the evacuation, patients were monitored with weekly β-hCG tests until remission was achieved and continued monthly for six months.

Statistical Analysis

All data were recorded systematically in preformed data collection form. Quantitative data was expressed as mean and standard deviation; qualitative data was expressed as frequency distribution and percentage. Statistical comparisons between groups were conducted using chi-square tests, while multivariate logistic regression was utilized to determine potential risk factors for persistent GTN, with adjustments for confounding variables. A p-value <0.05 was considered as significant. Statistical analysis was performed using SPSS 20.0 (Statistical Package for Social Sciences) for Windows version 10. The study was approved by the Institutional Review Board (IRB) of BSMMU.

Results

This table presents that a significant proportion (71.4%) of GTN-positive cases were younger than 20 years old, compared to only 16.3% in the GTN-negative group. No GTN-positive cases were observed in the 20–40 age range, whereas 37.2% of GTN-negative cases fell within this category. The mean age of GTN-positive cases (25 ± 11.28 years) was significantly lower than that of GTN-negative cases (34.28 ± 9.59 years), with a p-value of 0.024, indicating a statistically significant difference. All GTN-positive cases (100%) were classified as underweight (BMI < 18.5), compared to 48.8% of GTN-negative cases. No GTN-positive cases were observed in the normal weight (18.5–24.5) or overweight (24.5–29.9) categories, whereas 41.9% and 9.3% of GTN-negative cases fell into these categories, respectively. The difference in BMI distribution between the groups was statistically significant (p = 0.012) (Table 1).

Table 1: Association of GTN Status with Age and basal metabolic index (n=50)

Age (Years)	GTN Positive (n=7)	GTN Negative (n=43)	P-value
<20	5 (71.4%)	7 (16.3%)	
20-40	0 (0.0%)	16 (37.2%)	
>40	2 (28.6%)	20 (46.5%)	
Mean ± SD	25 ± 11.28	34.28 ± 9.59	0.024
Basal metabolic Index			
Underweight (<18.5)	7(100.0%)	21(48.8%)	0.012
Normal weight(18.5-24.5)	0	18(41.9%)	
Overweight (24.5-29.9)	0	4(9.3%)	

The duration of PV bleeding of patients was 0-2 weeks in 6(85.7%) of GTN positive and 43(100.0%) of GTN negative cases. Almost all of the patients, 6 (85.7%) and 43(100.0%) had lower abdominal pain in both groups accordingly. H/O Abortions were absent in 7(100.0%) mostly in GTN positive.H/O expulsion of grape-like vesicles was found in all 7(100.0%) and 26(60.5%) in both groups. Gestational age was 8-12 weeks mostly in 4(57.1%) of GTN positive and of 22(51.1%) GTN negative patients. All 7(100.0%) of the GTN-positive patients had vesicle size>2 cm. Almost three-fourths (71.4%) of the subjects had H/O mole in previous pregnancy in GTN positive and 9(20.9%) in GTN negative cases. The majority of the subjects had a history of thyrotoxic features 6(85.7%) and 11(25.6%) in both groups respectively. The difference in H/O Abortion, H/O expulsion of grape-like vesicle, size of the vesicle, H/O mole in a previous pregnancy, thyrotoxic feature, and family history of molar pregnancy were statistically significant (P<0.05) between GTN positive and GTN negative patients (Table 2).

Table 2: Distribution of Study Subjects by Presenting Symptoms (n=50)

Presenting symptom	GTN Positive (n=7)		GTN Negative (n=43)		*P-value*
	n	%	N	%	
Duration of PV bleeding					
0-2 Weeks	6	85.7	43	100	0.14
>6 months	1	14.3	0	0	
Lower abdominal pain	6	85.7	41	95.3	0.319
H/O Abortion	0	0	17	39.5	0.041
H/O Expulsion of grape-like vesicle	7	100	26	60.5	0.041
Size of the vesicle					
>1cm	0	0	33	76.7	0.001
>2cm	7	100	10	23.3	
Gestational age					
0-8 weeks	2	28.5	20	46.5	
8-12 weeks	4	57.1	22	51.1	0.268
>12 weeks	1	14.2	1	2.3	
H/O Thyrotoxic feature	6	85.7	11	25.6	0.001
H/O mole in previous pregnancy	5	71.4	9	20.9	0.005
Family history of molar pregnancy					
Molar pregnancy	4	57.1	0	0	
Choriocarcinoma	1	14.2	0	0	0
No	2	28.5	43	100	

GTN: Gestational Trophoblastic Neoplasia, PV bleeding: per vaginal bleeding

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Table 3 shows that 4 (57.1%) patients of the GTN-positive subjects were multiparous (>3 parity), compared to 14 (32.6%) in the GTN-negative group. The difference in parity between the two groups was statistically significant ($p < 0.05$). Most of the GTN-positive patients (71.4%), had vesicles with a cystic appearance in the USG of the uterus. Theca lutein cysts were also observed in 5 (71.4%) of the GTN-positive patients. The size of the theca lutein cysts was >6 cm in 4 (57.1%) of the GTN-positive patients. The differences in the vesicular and cystic appearance of uterine contents, as well as the size of the theca lutein cysts, were statistically significant ($p < 0.05$) between the GTN-positive and GTN-negative groups (Table 3).

Table 3: Association of GTN Status with Parity & USG findings (n=50)

Parity	GTN Positive (n=7)		GTN Negative (n=43)		P-value
	n	%	n	%	
0	3	42.9	8	18.6	0.049
1-3	0	0	21	48.8	
>3	4	57.1	14	32.6	
USG of uterus					
Vesicular	3	42.8	23	53.5	0.005
Cystic	2	28.6	18	41.8	
Snowstorm appearance	0	0	2	4.7	
Necrotic	2	28.6	0	0	
USG of ovary					
Normal	2	28.6	27	62.8	0.088
Theca lutein cyst	5	71.4	16	37.2	
Size of theca lutein cyst					
<6 cm	1	14.3	9	20.9	0.029
>6 cm	4	57.1	6	14	
No cyst	2	28.6	28	65.1	

GTN: Gestational Trophoblastic Neoplasia, USG: Ultrasonogram

The β-hCG mean at 1st, 2nd, 3rd, and 4th weeks was almost alike in GTN positive and negative. The mean β-hCG in the 5th week was 4.15±0.68 in GTN positive and 3.01±0.85 in GTN negative. The mean β-hCG in the 6th week was 4.09±0.76 in GTN positive and 2.41±0.91 in GTN negative. The mean β-hCG in the 7th week was 4.34±0.94 in GTN positive and 1.82±0.7 in GTN negative. The mean β-hCG in the 8th week was 3.99±1.18 in GTN positive and -1.31±0.77 in GTN negative. The differences in β-hCG levels in the 5th, 6th, 7th, and 8th weeks were statistically significant ($P<0.05$) between GTN-positive and GTN-negative (Table 4).

Table 4: Comparing the Mean of Log-Transformed ß-hCG Values at Different Time Points (n=50)

β-hCG	GTN Positive (n=7)	GTN Negative (n=43)	p-value
	Mean±SD	Mean±SD	
β-hCG in1st week	4.68±0.49	4.69±0.42	0.954
β-hCG in 2nd week	4.32±0.54	4.37±0.59	0.834
β-hCG in 3rd week	4.12±0.51	3.88±0.71	0.396
β-hCG in 4th week	4.04±0.74	3.47±0.78	0.077
β-hCG in 5th week	4.15±0.68	3.01±0.85	0.001
β-hCG in 6th week	4.09±0.76	2.41±0.91	0.001
β-hCG in 7th week	4.34±0.94	1.82±0.7	0.001
β-hCG in 8th week	3.99±1.18	-1.31±0.77	0.001

Table 5 showed that ß-hCG with a cutoff value ≥4.60 predicts PGTN with a sensitivity of 71.4% and specificity of 27.9% having area under the curve (AUC) = 0.513 in the first week after evacuation and the sensitivity and specificity of ß-hCG increased in subsequent follow-up weeks after evacuation for the prediction of GTN. The table displayed the obtained sensitivity, specificity, and AUC from the ROC curve analysis for the estimated probabilities as well as the power of β hCG levels to predict PGTN, separately in weeks 0 to 8. The obtained indices (sensitivity, specificity, and AUC), based on the best cut-off points for the estimated probabilities, show the β-hCG levels from all weeks had the best power to predict PGTN (AUC = 99.7%). The sensitivity and specificity of ß-hCG have been increased in the subsequent 5th to 8th week after evacuation for the prediction of PGTN (Table 5).

Table 5: Power of Log-Transformed ß-hCG Values for Predicting GTN at Different Time Points (n=50)

Weeks	Cutoff value	Sensitivity	Specificity	AUC
ß-hcg 1wk	4.6	71.4	27.9	0.513
ß-hcg 2wk	4.61	71.4	37.2	0.505
ß-hcg 3wk	4.45	74.4	42.9	0.601
ß-hcg 4wk	4.06	79.1	57.1	0.698
ß-hcg 5wk	3.7	83.7	71.4	0.852
ß-hcg 6wk	3.63	86	75.1	0.907
ß-hcg 7wk	2.62	86	85.7	0.977
ß-hcg 8wk	1.59	97.7	100	0.997

GTN: Gestational Trophoblastic Neoplasia, ß-hCG: beta-human chorionic gonadotropin, AUC: Area Under Curv

The multivariate logistic regression analysis indicates that age is significantly associated with the development of GTN ($p<0.05$). Younger age was found to significantly increase the risk of developing GTN, with an odds ratio of 1.17 (95%

CI: 1.02 – 16.3). However, a history of a mole in a previous pregnancy, thyrotoxic features, and uterine size per abdomen were not significantly associated with persistent gestational trophoblastic neoplasia (PGTN) in the multivariate logistic regression model (Table 6).

Figure 1 shows the ROC Curves of Log-Transformed ß-hCG Values for predicting GTN at Different Time Points from the 5th week to the 8th week. In the 5th week of analysis, the sensitivity of 83.7%, and the specificity of 71.4%, having an area under the curve (AUC = 0.852). In 6th week of analysis, a sensitivity of 86.0% and specificity of 75.1% had an area under the curve (AUC = 0.907). In the 7th week of analysis, a sensitivity of 86% and specificity of 85.7% having an area under the curve (AUC = 0.977), and in 8th week of analysis, a sensitivity of 97.7% and specificity of 100.0% having an area under the curve (AUC = 0.997) (Figure 1).

Table 6: Multivariate Logistic Regression Analysis for Risk Factors of Persistent Gestational Trophoblastic Neoplasia (n=50)

Characteristics	B	S.E.	P value	OR	95% C.I.	
					Lower	Upper
Age	0.16	0.07	0.03	1.17	1.02	16.35
H/O mole in previous pregnancy	2.01	1.57	0.199	0.48	0.35	1.93
Thyrotoxic feature	1.39	1.53	0.363	0.03	0.2	1.05
Uterus size per abdomen	2.56	1.64	0.119	0.88	0.52	2.94

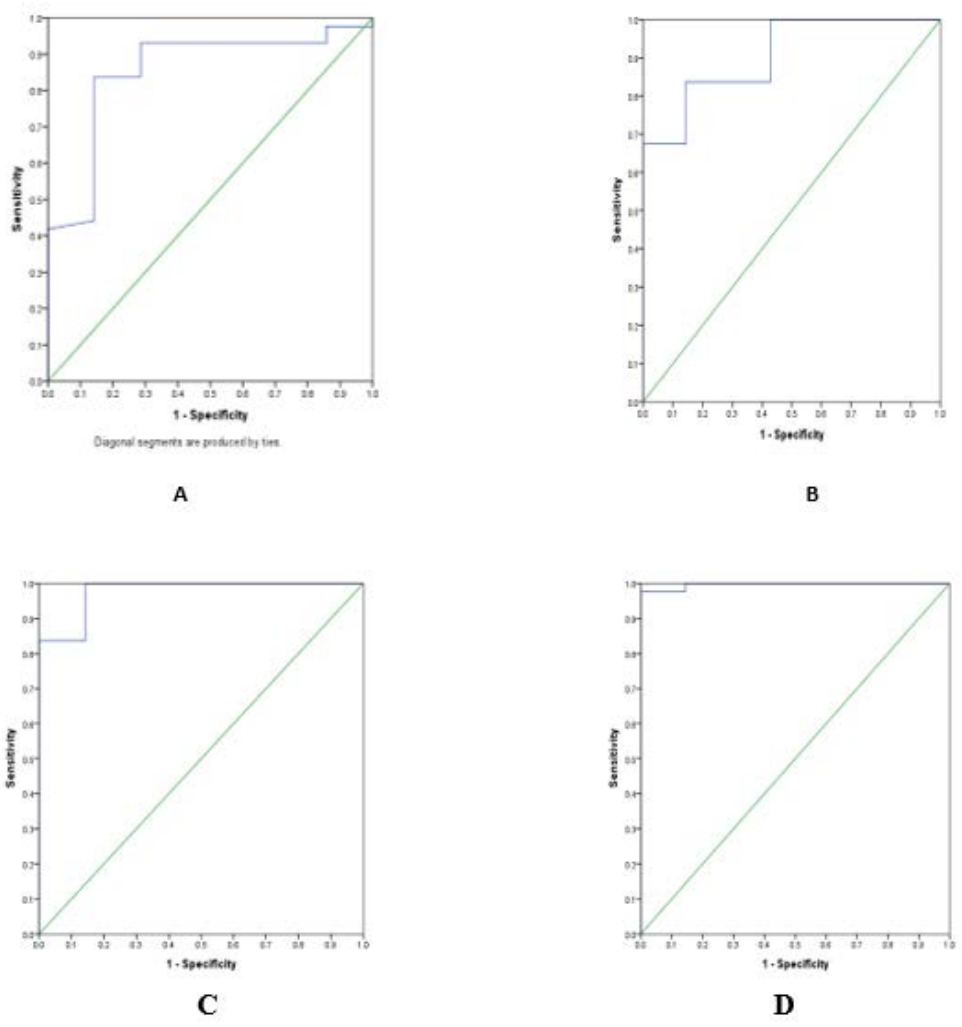

Figure 1: Estimated ROC Curves of Log-Transformed ß-hCG Values for Predicting GTN at 5th week (A), 6th week (B), 7th week (C) and 8th week (D)

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Discussion

The present study found that a significant portion of GTN-positive patients (71.4%) were under the age of 20, compared to 16.3% in the GTN-negative group. The mean age was 25 years for GTN-positive patients and 34.28 years for GTN-negative patients ($p < 0.05$). These results align with Capobianco et al.'s study also identified younger age as a significant risk factor for Gestational Trophoblastic Disease (GTD), underscoring the importance of age in GTN development and persistence [16].

In our study, 57.1% of the PGTN-positive group, were multipara (parity >3), compared to 14 (32.6%) in the PGTN-negative group. Multiparity was strongly associated with the development of PGTN ($p = 0.049$) in this study. A study conducted at Rajshahi Medical College Hospital found that 81.2% of patients were multipara [17]. Another study showed that hydatidiform mole was associated with multiparity in 60% of cases [18]. Most of the patients, 5 (71.4%), in the PGTN-positive group showed a vesicular cystic appearance on ultrasound of the uterus, which was associated with the development of persistent GTN ($p = 0.005$). In a study, a cystic snowstorm appearance on ultrasound was observed in 37.1% of cases and was significantly associated with the development of PGTN ($p = 0.005$) [19]. The majority (71.4%) of patients in the GTN group had theca lutein cysts in the ovary ($p = 0.008$). The size of the theca lutein cysts was >6 cm in 4 (57.1%) of the GTN group, which was significant in the development of PGTN. A study showed that >6 cm theca lutein cysts were present in 15 (17.6%) of study subjects [20].

The uterine size was measured per abdominally and showed more than a period of gestation in 6(85.7%) of the GTN positive group and 13(30.2%) in the GTN negative group. The size of the uterus per abdomen was significantly associated with the development of persistent GTN (P=.043). In a study, uterine size was more than the period of gestation in 22 (78.6%) which showed a similar association with PGTN development [21]. Another study revealed 50% of the patients had a uterine size larger than the period of gestation [22].

In the present study, it was observed that β-hCG initial post-evacuation was greater than 100000 in all cases of PGTN positive and 21 (48.8%) in PGTN negative. β-hCG was significantly associated with the development of persistent GTN in this study. A study evaluated the initial post-evacuation serum hCG among 23(62%) patients which was greater than 100000 mIU/ml and was significantly associated with the development of PGTN [23]. A similar association was found in a study in 16(72.7%) patients where β-hcg initial was > 100,000 ml/U [22].

In this study, the descriptive statistics were done for β-hCG levels as well as P values for comparing the mean β-hCG between women with and without PGTN at different time points(1^{st} to 8^{th} weeks) after molar evacuation in women with hydatidiform mole. Reported P values indicated that the difference between mean β-hCG values in all groups was not significantly associated at the first to fourth weeks but significant association was observed in the 5^{th} to 8^{th} weeks (P=.001). The results suggested that the values of this biomarker in weeks 5 to 8 had more predictive power for discriminating women with and without PGTN. In a study, it was reported that the median β-hCG level 2 weeks after evacuation in the patients with PGTN was significantly higher than in the remission group [24]. In another study, a rising titer is defined as increasing levels based on two or more consecutive weekly measurements. Persistent is when elevation of β-hCG titers is found after 16 weeks of evacuation [20].

Most of the patients whose β-hCG titers were more than 1000 mIU/ml in the 5th week after the first evacuation developed subsequently from persistent trophoblastic disease. In more than 90% of the spontaneous resolution cases, their hCG titers decreased to less than 100 mIU/ml in the 8th week. These findings indicated that the hCG titers at the 5th, 8th, and 20th weeks after the first evacuation were crucial for predicting persistent trophoblastic disease [25]. Another study suggested that free β- hCG concentrations increased rapidly, reaching maximum values at 8-9 weeks of gestation and then declining gradually during the following 11-12 weeks [26].

In this study, sensitivity, specificity, and AUC from the ROC curve analysis were considered separately in weeks 0-8 for the estimated probabilities as well as the power of ß-hCG levels to predict PGTN. The obtained results showed that more than 97% of women with PGTN could be classified correctly, 5-8 week trend of ß-hCG concentration after mole evacuation in the current study. A study was conducted where hCG regression rate (hCG divided by initial hCG) could predict the PGTN with a sensitivity of 48.0% and specificity of 89.5%(AUC = 0.759) in the second week after evacuation. In their study, only the patients with an initial hCG level of more than 100,000 IU/L were investigated [24].

The age of the patients was significantly associated with the development of PGTN in multivariate logistic regression analysis ($p < 0.05$). Younger age significantly increased the risk of developing PGTN by 1.17 times ($p < 0.05$), with a 95% confidence interval (CI) of 1.02 – 16.35%. One study identified age (RR = 2.87) and history of mole (RR = 2.57) as the most powerful indicators of persistent disease after multivariate analysis [13]. Another study found that pre-evacuation β-hCG levels ≥ 134,182.5 mIU/ml were a risk factor for gestational trophoblastic neoplasia (OR =77.008,

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p = 0.004) [27]. Additionally, histopathologic features, uterine size, lutein cysts >6 cm, and pre-evacuation β-hCG levels were predictors of persistent gestational trophoblastic neoplasia [23].

Our study has some limitations. The study was a single-center study. We took a small sample size due to the short study period, so it may not fully represent broader populations with different genetic, environmental, or healthcare factors. After evaluating those patients, multiple risk factors were analyzed, but other potential predictors, such as genetic predisposition and hormonal influences, were not included.

Conclusion and Recommendations

This study highlights key risk factors for the development of persistent gestational trophoblastic neoplasia (PGTN) in patients with hydatidiform moles. Younger age, lower BMI, larger vesicle size, and persistently elevated β-hCG levels (weeks 5–8) were significantly associated with an increased risk of GTN. Multivariate analysis confirmed that younger age independently contributed to a greater likelihood of developing GTN. However, factors such as a history of molar pregnancy, thyrotoxic features, and uterine size were not significantly associated with GTN in the adjusted model.

Future research with larger, multicenter, and prospective study designs including a larger sample size is needed to validate these findings and explore additional genetic or molecular markers for GTN prediction.

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References

1. Altieri A, Franceschi S, Ferlay J, Smith J, et al. Epidemiology and etiology of gestational trophoblastic diseases. Lancet Oncol 4 (2003): 670–8.
2. Jagtap SV, Aher V, Gadhiya S, et al. Gestational trophoblastic disease—Clinicopathological study at tertiary care hospital. J Clin Diagn Res 11 (2017): EC27.
3. Berkowitz RS, Goldstein DP. Gestational trophoblastic disease. Cancer 76 (1995): 2079-85.
4. Garner EI, Goldstein DP, Feltmate CM, Berkowitz RS. Gestational trophoblastic disease. Clin Obstet Gynecol 50 (2007): 112–22.
5. Grimes DA. Epidemiology of gestational trophoblastic disease. Am J Obstet Gynecol 150 (1984): 309-18.
6. Nizam K, Haider G, Memon N, Haider A. Gestational trophoblastic disease: experience at Nawabshah Hospital. J Ayub Med Coll Abbottabad 21 (2009): 94–7.
7. Lurain JR. Gestational trophoblastic disease II: classification and management of gestational trophoblastic neoplasia. Am J Obstet Gynecol 204 (2011): 11–8.
8. de Mello JB, Cirilo PD, Michelin OC, Domingues MA, et al. Genomic profile in gestational and non-gestational choriocarcinomas. Placenta 50 (2017): 8–15.
9. Rahman SKP, Sudhamani C. Incidence and risk factors of post-molar gestational trophoblastic neoplasia—A prospective study. Int J Reprod Contracept Obstet Gynecol 12 (2023): 924–30.
10. Loh KY, Sivalingam N, Suryani MY. Gestational trophoblastic disease. Med J Malaysia 59 (2004): 697–703.
11. Mousavi AS, Karimi S, Modarres Gilani M, Akhavan S, et al. Does post-evacuation β-human chorionic gonadotropin level predict persistent gestational trophoblastic neoplasia? Int Schol Res Notices (2014).
12. Goldstein DP, Berkowitz RS, Bernstein MR. Management of molar pregnancy. J Reprod Med 26 (1981): 208–12.
13. Ayhan A, Tuncer ZS, Halilzade H, et al. Predictors of persistent disease in women with complete hydatidiform mole. J Reprod Med 41 (1996): 591–4.
14. Schlaerth JB, Morrow CP, Kletzky OA, Nalick RH, et al. Prognostic characteristics of serum human chorionic gonadotropin titer regression following molar pregnancy. Obstet Gynecol 58 (1981): 478–82.
15. Shigematsu T, Kamura T, Saito T, Kaku T, et al. Identification of persistent trophoblastic diseases based on a human chorionic gonadotropin regression curve by means of a stepwise piecewise linear regression analysis after the evacuation of uneventful moles. Gynecol Oncol 71 (1998): 376-80.
16. Capobianco G, Tinacci E, Saderi L, Dessole F, et al. High Incidence of Gestational Trophoblastic Disease in a Third-Level University-Hospital, Italy: A Retrospective Cohort Study. Front Oncol 11 (2021): 684700.
17. Shamima MN, Zereen R, Hossain MA, Zahan N, et al. Evaluation of molar pregnancy in Rajshahi Medical College Hospital. KYAMC J 9 (2018): 24–7.
18. Mungan T, Kuşçu E, Dabakoğlu T, Senöz S, et al. Hydatidiform mole: clinical analysis of 310 patients. Int J Gynaecol Obstet 52 (1996): 233-6.
19. Al Riyami N, Al Riyami M, Al Hajri AT, Al Saidi S, et al. Gestational Trophoblastic Disease at Sultan Qaboos University Hospital: Prevalence, Risk Factors,

Histological Features, Sonographic Findings, and Outcomes. Oman Med J 34 (2019): 200-204.

20. Fatima M, Kasi PM, Baloch SN, Kassi M, et al. Incidence, management, and outcome of molar pregnancies at a tertiary care hospital in Quetta, Pakistan. Int Schol Res Notices (2011): 925316.

21. Bindu P, Nair P. Effect of pre-evacuation serum β-hCG levels on post-evacuation β-hCG regression in molar pregnancy. J Med Sci Clin Res 5 (2017): 21734–40.

22. Mulik J, Choudhary A. Clinical study of gestational trophoblastic disease in a tertiary care hospital. Int J Reprod Contracept Obstet Gynecol 9 (2020): 2964-8.

23. Shrivastava S, Gandhewar MR. Gestational trophoblastic disease: A profile of 37 cases. Int J Reprod Contracept Obstet Gynecol 3 (2014): 317–21.

24. Kang WD, Choi HS, Kim SM. Prediction of persistent gestational trophobalstic neoplasia: the role of hCG level and ratio in 2 weeks after evacuation of complete mole. Gynecol Oncol 124 (2012): 250-3.

25. Sasaki S. Clinical presentation and management of molar pregnancy. Best Pract Res Clin Obstet Gynaecol 17 (2003): 885-92.

26. Rangwala TH, Badawi F. A profile of cases of gestational trophoblastic neoplasia at a large tertiary centre in Dubai. ISRN Obstet Gynecol (2011): 453190.

27. Saputra AN, Shaleh AZ, Agustiansyah P, et al. Malignancy risk factors of hydatidiform mole. Indones J Obstet Gynecol (2019): 146–51.

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