

# Serum $\beta$ -hCG Trends and Their Clinical Significance in Persistent Gestational Trophoblastic Neoplasia

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## ABSTRACT

**Background:** Persistent gestational trophoblastic neoplasia (PGTN) is characterized by abnormal trophoblastic proliferation with persistently elevated or abnormal serum  $\beta$ -hCG levels. Serial  $\beta$ -hCG monitoring is crucial for assessing disease activity, treatment response, and prognosis. Aim of the study: To evaluate serum  $\beta$ -hCG trends and determine their clinical significance in predicting persistence, treatment response, and prognosis in PGTN patients. **Methods & Materials:** This cross-sectional study was conducted in the Department of Gynecological Oncology, BSMMU, Bangladesh (January–December 2021). A total of 50 PGTN patients were included. Serial serum  $\beta$ -hCG levels, clinical characteristics, FIGO risk scores, metastatic status, and treatment outcomes were analyzed using SPSS version 20. Chi-square tests and logistic regression were applied. **Result:** All patients (100%) presented with initial  $\beta$ -hCG  $>10^5$  mIU/mL. Declining  $\beta$ -hCG trends were observed in 88%, plateau in 6%, and rising in 6%. Complete remission occurred in 100% of patients with declining trends, while persistent disease (66.67%) and recurrence (33.33%) were seen in plateau/rising groups ( $p=0.001$ ). High FIGO risk score (OR 4.21, 95% CI: 1.58–10.92), metastasis (OR 6.78, 95% CI: 1.44–32.60), and plateau/rising  $\beta$ -hCG trends (OR 5.64, 95% CI: 2.10–12.80) were significant predictors of poor outcome. **Conclusion:** Serial serum  $\beta$ -hCG trends are highly predictive of clinical outcomes in PGTN. A declining  $\beta$ -hCG pattern is strongly associated with complete remission, while plateau or rising trends significantly indicate persistent disease and recurrence. High FIGO risk score, metastatic disease, and elevated baseline  $\beta$ -hCG further increase the likelihood of treatment failure. Early

recognition of abnormal  $\beta$ -hCG kinetics enables timely intervention and improves prognosis. Routine and structured  $\beta$ -hCG monitoring should be considered an essential component of PGTN management protocols to enhance risk stratification, guide chemotherapy decisions, and optimize long-term survival outcomes in affected patients.

**Keywords:** Gestational trophoblastic neoplasia,  $\beta$ -hCG, persistent disease, FIGO score, chemotherapy response, prognosis.

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## INTRODUCTION

Gestational trophoblastic neoplasia (GTN) is a malignant form of gestational trophoblastic disease arising from abnormal proliferation of placental trophoblastic tissue, usually following a molar pregnancy, abortion, or normal gestation, and is characterized by persistently elevated or rising serum  $\beta$ -hCG levels indicating active disease and tumor burden [1]. Globally, the incidence of GTN varies widely, ranging approximately from 1 to 0.02/0.07 cases per 1000 pregnancies, with higher rates reported in parts of Asia and other developing regions [2]. In Bangladesh, GTN accounts for approximately 5%-25% of all gestational trophoblastic disease (GTD) cases. Among treated molar pregnancies, about 15%-25% may progress to persistent GTN requiring chemotherapy and follow-up  $\beta$ -hCG monitoring in tertiary care settings [3]. The disease process begins when abnormal trophoblastic tissue continues to proliferate after uterine evacuation, leading to persistently elevated or rising serum  $\beta$ -hCG levels due to ongoing production by viable or residual trophoblastic cells. Serum  $\beta$ -hCG measurement is therefore essential for monitoring disease activity and

treatment response. A plateau, defined as minimal change over time, or a secondary rise after an initial decline, strongly suggests persistent gestational trophoblastic neoplasia or resistance to therapy. These abnormal trends help distinguish normal post-evacuation recovery from active disease, guiding early intervention and preventing progression to metastatic complications or treatment delay [4]. This monitoring process is based on repeated quantitative  $\beta$ -hCG measurements, which provide a highly sensitive indicator of trophoblastic activity compared to early imaging modalities. Rising or plateauing  $\beta$ -hCG levels suggest persistent or active neoplastic disease, whereas a consistent decline reflects effective treatment response and progression toward remission. Serial trends play a crucial role in early detection of treatment failure and in guiding timely clinical intervention in gestational trophoblastic neoplasia [5]. Early detection of abnormal  $\beta$ -hCG trends enables prompt initiation of chemotherapy, which prevents metastatic spread and significantly impacts treatment outcomes. With close monitoring, GTN becomes one of the most highly curable gynecological malignancies, with

markedly improved long-term survival rates [6,7]. Serial  $\beta$ -hCG monitoring is a non-invasive, cost-effective, and sensitive method for early detection of persistent or recurrent disease in gestational trophoblastic neoplasia, enabling timely therapeutic intervention. This approach supports individualized treatment strategies and improves clinical outcomes by reducing disease-related mortality [8]. However, disadvantages include psychological stress from prolonged follow-up, false-positive fluctuations, and dependency on patient compliance for serial testing [9]. Improving early detection of persistent disease, optimizing follow-up strategies, and reducing delayed diagnosis of resistant GTN are essential for better survival and fertility preservation [10]. Despite advances, limitations in existing research include single-center data, inconsistent follow-up protocols, and limited long-term outcome analysis, particularly in low-resource settings [11]. Therefore, there is a need for the current study to better define  $\beta$ -hCG trend patterns, improve risk stratification, and strengthen evidence-based monitoring strategies for persistent GTN in diverse populations. The objective of this study was

to evaluate serum  $\beta$ -hCG trends and determine their clinical significance in predicting persistence, treatment response, and prognosis in patients with gestational trophoblastic neoplasia.

**METHODS & MATERIALS**

This cross sectional study was conducted in the Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU) in Bangladesh. The study spanned 1 years, from January 2021 to December 2021, and focused on patients diagnosed with Persistent Gestational Trophoblastic Neoplasia (PGTN). Using a purposive sampling method, a total of 50 patients attending the department were enrolled, forming a clearly defined study cohort. Participants were selected according to predefined inclusion and exclusion criteria to ensure the validity and clinical relevance of the study. Patients were included following confirmation of Persistent Gestational Trophoblastic Neoplasia based on clinical evaluation, serial serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) monitoring, ultrasonographic findings, and diagnostic criteria according to the International Federation of Gynecology and Obstetrics (FIGO) guidelines.

**Inclusion Criteria**

- Patients diagnosed with Persistent Gestational Trophoblastic Neoplasia.
- Patients aged 18 years or older.

- Patients with available serial serum  $\beta$ -hCG follow-up records.
- Patients who provided informed written consent to participate in the study.

**Exclusion Criteria**

- Patients with incomplete medical records or missing serial  $\beta$ -hCG measurements.
- Patients with concurrent gynecological malignancies.
- Patients with severe systemic illnesses interfering with treatment response assessment.
- Patients unwilling to participate in the study.

**Data Collection**

Data were systematically collected using a structured data collection sheet and hospital medical records. Socio-demographic and reproductive variables including age, residence, parity, previous history of molar pregnancy, and type of antecedent pregnancy were documented. Clinical presentation variables such as irregular vaginal bleeding, amenorrhea, pelvic pain, hyperemesis, FIGO risk score, disease stage, and presence of metastatic disease were also recorded.

Baseline serum  $\beta$ -hCG levels were measured at diagnosis and serial  $\beta$ -hCG trends during follow-up were evaluated to determine declining, plateau, rising, or fluctuating patterns. Time to  $\beta$ -hCG normalization was documented. Treatment outcomes including complete remission,

persistent disease, recurrence, and response to chemotherapy were assessed to determine the clinical significance of serum  $\beta$ -hCG trends in Persistent Gestational Trophoblastic Neoplasia.

**Statistical Analysis**

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) software version 20. Continuous variables were expressed as mean  $\pm$  standard deviation (SD), while categorical variables were summarized as frequencies and percentages. The chi-square test was applied to assess associations between serum  $\beta$ -hCG trends and clinical outcomes. Logistic regression analysis was performed to identify predictors of persistent disease, and results were expressed as odds ratio (OR) with 95% confidence interval (CI). A p-value  $\leq 0.05$  was considered statistically significant.

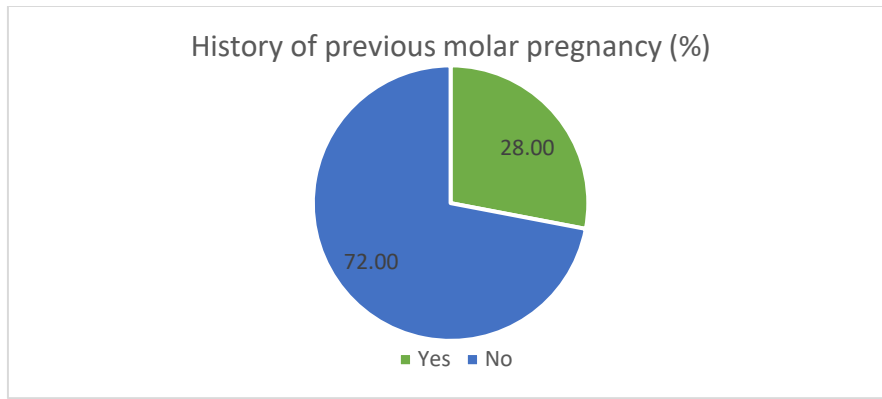
**RESULT**

A total of 50 patients with persistent gestational trophoblastic neoplasia (GTN) were included in this study. The highest proportion of patients was in the age group  $>40$  years (44.00%), followed by  $\leq 20$  years (24.00%), 21–30 years (20.00%), and 31–40 years (12.00%). Regarding residence, 64.00% of patients were from rural areas, while 36.00% were from urban areas. In terms of parity, multiparous women constituted the majority (54.00%), followed by primiparous (24.00%) and nulliparous (22.00%) patients (Table I).

**Table I**

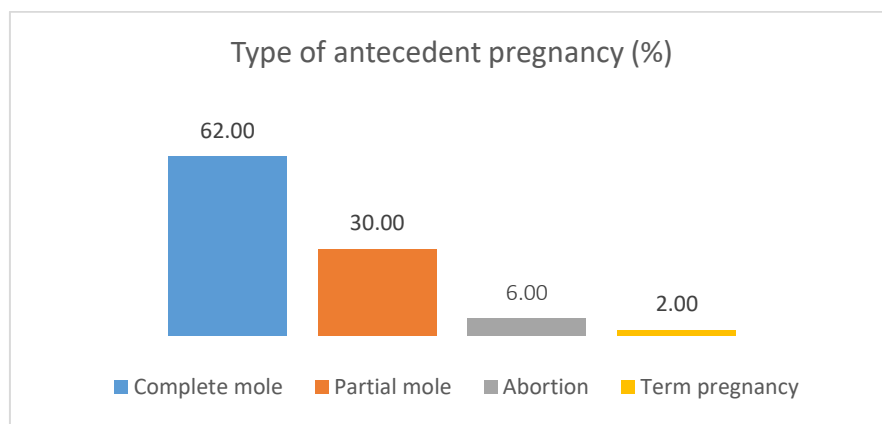
Baseline Socio-demographic and Reproductive Characteristics of Patients with Persistent Gestational Trophoblastic Neoplasia ( $n = 50$ ).

Baseline Characteristics	Frequency (n)	Percentage (%)
Age group (years)		
$\leq 20$	12	24.00
21–30	10	20.00
31–40	6	12.00
$>40$	22	44.00
Residence		
Urban	18	36.00
Rural	32	64.00
Parity		
Nulliparous	11	22.00
Primiparous	12	24.00
Multiparous	27	54.00



**Figure 1** History of previous molar pregnancy (n=50).

A history of previous molar pregnancy was present in 28.00% of cases, whereas 72.00% had no documented history of molar pregnancy (Figure 1).



**Figure 2** Type of antecedent pregnancy (n=50).

Figure 2 illustrated that 62.00% of antecedent pregnancies were complete mole, 30.00% were partial mole, 6.00% followed abortion, and 2.00% followed term pregnancy.

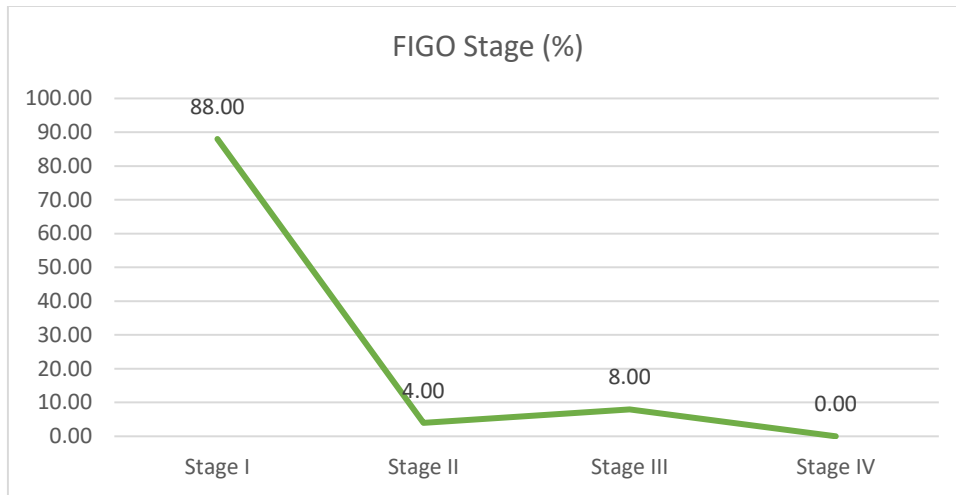
All patients (100.00%) presented with irregular vaginal bleeding. Pelvic pain was reported in 94.00% of cases, amenorrhea in 76.00%, and hyperemesis in 28.00%. Only 4.00% of patients were asymptomatic and were detected during follow-up serum  $\beta$ -hCG monitoring. Regarding FIGO risk

stratification, 90.00% of patients were classified as low risk ( $<7$ ), while 10.00% were high risk ( $\geq 7$ ). Metastatic disease was present in 4.00% and absent in 96.00% of cases (Table II).

**Table II**

Clinical Presentation and Baseline Disease Characteristics of Persistent Gestational Trophoblastic Neoplasia (n = 50).

Clinical Characteristics	Frequency (n)	Percentage (%)
<b>Presenting symptoms</b>		
Irregular vaginal bleeding	50	100.00
Amenorrhea	38	76.00
Pelvic pain	47	94.00
Hyperemesis	14	28.00
Asymptomatic (detected by follow-up $\beta$ -hCG)	2	4.00
<b>FIGO risk score</b>		
Low risk ( $<7$ )	45	90.00
High risk ( $\geq 7$ )	5	10.00
<b>Metastatic disease</b>		
Present	2	4.00
Absent	48	96.00



**Figure 3** FIGO Stages of the patients (n=50).

FIGO staging showed that 88.00% of patients were in Stage I, 4.00% in Stage II, 8.00% in Stage III, and 0.00% in Stage IV (Figure 3).

All patients (100.00%) had initial serum  $\beta$ -hCG levels  $>10^5$  mIU/mL. During follow-up, 88.00% showed a declining trend, 6.00% plateaued, and 6.00% showed a rising pattern. None demonstrated a fluctuating pattern. Regarding time to

normalization, 56.00% achieved  $\beta$ -hCG normalization within  $<8$  weeks, 30.00% within 8–12 weeks, and 14.00% required  $>12$  weeks (Table III).

**Table III**

Baseline Serum  $\beta$ -hCG Levels and Serial Trends Among Patients with Persistent Gestational Trophoblastic Neoplasia (n =50).

$\beta$ -hCG Related Variables	Frequency (n)	Percentage (%)
Initial serum $\beta$ -hCG level (mIU/mL)		
$<10^3$	0	0
$10^3$ – $10^4$	0	0
$10^4$ – $10^5$	0	0
$>10^5$	50	100
$\beta$ -hCG trend during follow-up		
Declining	44	88
Plateau	3	6
Rising	3	6
Fluctuating	0	0
Time to $\beta$ -hCG normalization		
$<8$ weeks	28	56
8–12 weeks	15	30
$>12$ weeks	7	14

Declining  $\beta$ -hCG was strongly associated with low-risk disease (95.45%), absence of metastasis (100.00%), and complete remission (100.00%), whereas plateau or

rising  $\beta$ -hCG was associated with high-risk disease (50.00%), metastatic disease (33.33%), persistent disease (66.67%), and

recurrence (33.33%) (all  $p=0.001$ – $0.003$ ) (Table IV).

**Table IV**

Association between Serum  $\beta$ -hCG Trends and Clinical Outcomes in Persistent Gestational Trophoblastic Neoplasia.

Characteristics	Declining $\beta$ -hCG n (%)	Plateau/Rising $\beta$ -hCG n (%)	P value
FIGO risk category			
Low risk	42 (95.45)	3 (50.00)	0.001
High risk	2 (4.55)	3 (50.00)	0.001
Metastatic disease			
Present	0 (0.00)	2 (33.33)	0.003
Absent	44 (100.00)	4 (66.67)	0.003
Chemotherapy response			
Complete remission	44 (100.00)	0 (0.00)	0.001
Persistent disease	0 (0.00)	4 (66.67)	0.001
Recurrence	0 (0.00)	2 (33.33)	0.001

Table V demonstrated that patients with baseline  $\beta$ -hCG  $>10^5$  mIU/mL had complete

remission in 88.00%, persistent disease in 8.00%, and recurrence in 4.00% ( $p=0.001$ ).

**Table V**  
Relationship Between Baseline Serum  $\beta$ -hCG Level and Treatment Outcome in Persistent Gestational Trophoblastic Neoplasia.

Baseline $\beta$ -hCG Level	Complete Remission n (%)	Persistent Disease n (%)	Recurrence n (%)	P value
<10 <sup>3</sup> mIU/mL	0 (0.00)	0 (0.00)	0 (0.00)	0.001
10 <sup>3</sup> -10 <sup>4</sup> mIU/mL	0 (0.00)	0 (0.00)	0 (0.00)	
10 <sup>4</sup> -10 <sup>5</sup> mIU/mL	0 (0.00)	0 (0.00)	0 (0.00)	
>10 <sup>5</sup> mIU/mL	44 (88.00)	4 (8.00)	2 (4.00)	

Table VI shows logistic regression analysis identifying significant predictors of persistent disease, including age >30 years (OR 1.17, p=0.03), high baseline  $\beta$ -hCG >10<sup>5</sup> mIU/mL (OR 3.92, p=0.001), plateau/rising  $\beta$ -hCG trend (OR 5.64, p=0.001), high FIGO risk score (OR 4.21, p=0.002), and presence of metastasis (OR 6.78, p=0.003) (Table VI).

**Table VI**  
Predictors of Persistent Disease According to Logistic Regression Analysis.

Characteristics	OR	95% C.I.	P value
Age (>30 years)	1.17	1.02-16.35	0.03
High baseline $\beta$ -hCG (>10 <sup>5</sup> mIU/mL)	3.92	1.71-8.97	0.001
Plateau/rising $\beta$ -hCG trend	5.64	2.10-12.80	0.001
High FIGO risk score	4.21	1.58-10.92	0.002
Presence of metastasis	6.78	1.44-32.60	0.003

**DISCUSSION**

Gestational trophoblastic neoplasia (GTN) represents a spectrum of malignant trophoblastic proliferation, where serum  $\beta$ -hCG remains the most sensitive biomarker for diagnosis, monitoring, and prognosis [12]. In the present study, we analyzed 50 patients with persistent GTN to evaluate  $\beta$ -hCG trends and their clinical significance in relation to disease characteristics and treatment outcomes. In our study, the highest proportion of patients belonged to the age group >40 years (44.00%), followed by  $\leq$ 20 years (24.00%), 21-30 years (20.00%), and 31-40 years (12.00%). This bimodal age distribution aligns with established evidence that both extremes of reproductive age carry increased risk for trophoblastic disease progression. Seckl et al. reported that advanced maternal age is associated with increased risk of malignant transformation and chemoresistance due to altered trophoblastic immune tolerance and genomic instability [13]. Parity analysis showed that multiparous women constituted 54.00%, followed by primiparous (24.00%) and nulliparous (22.00%) women. This pattern is similar to previous reports suggesting that repeated pregnancies may increase trophoblastic instability and risk of abnormal implantation [14]. A history of previous molar pregnancy was present in 28.00% of cases, while 72.00% had no such history. This finding emphasizes that although prior molar pregnancy is a strong risk factor, a substantial proportion of persistent GTN occurs without documented molar antecedent, as also reported in FIGO observational datasets [15]. The majority of antecedent pregnancies were complete mole (62.00%), followed by partial mole (30.00%), abortion (6.00%), and term pregnancy (2.00%). This distribution strongly supports existing literature

indicating that complete hydatidiform mole carries the highest malignant potential due to diffuse trophoblastic proliferation and androgenetic diploidy. Approximately 15-20% of complete moles may progress to GTN, compared to only 1-5% of partial moles [6,16]. Our findings further reinforce the dominant role of complete mole as the primary precursor lesion in persistent GTN. All patients (100.00%) presented with irregular vaginal bleeding, making it the universal clinical symptom in our cohort. Pelvic pain was present in 94.00% of cases, amenorrhea in 76.00%, hyperemesis in 28.00%, and only 4.00% were asymptomatic and detected through follow-up  $\beta$ -hCG monitoring. These findings are consistent with Kong et al. & Bruner et al., who reported abnormal uterine bleeding as the most consistent presenting feature of GTN, often accompanied by pelvic discomfort due to uterine invasion or distension [17,18]. A striking finding was that all patients (100.00%) had baseline serum  $\beta$ -hCG levels >10<sup>5</sup> mIU/mL, with no cases in lower categories (<10<sup>3</sup>, 10<sup>3</sup>-10<sup>4</sup>, or 10<sup>4</sup>-10<sup>5</sup> mIU/mL). This indicates a very high tumor burden at presentation and suggests delayed diagnosis or referral. Elevated baseline  $\beta$ -hCG has been consistently identified as a strong predictor of treatment resistance and poor prognosis in GTN [19]. Among patients with declining  $\beta$ -hCG, 95.45% were low-risk and 4.55% were high-risk. In contrast, among those with plateau/rising trends, only 50.00% were low-risk and 50.00% were high-risk (p=0.001). This highlights that abnormal  $\beta$ -hCG kinetics are strongly linked with higher-risk disease [20]. Treatment response showed a clear pattern: all patients with declining  $\beta$ -hCG achieved complete remission (100.00%), while none had persistent disease or recurrence. These findings strongly confirm that  $\beta$ -hCG trend

is a real-time predictor of therapeutic outcome, consistent with FIGO recommendations [21]. Baseline  $\beta$ -hCG level >10<sup>5</sup> mIU/mL was associated with complete remission in 88.00% of cases, while 8.00% developed persistent disease and 4.00% experienced recurrence (p=0.001). Although high remission was still observed, the presence of persistent and recurrent cases exclusively in this group emphasizes that extremely elevated baseline  $\beta$ -hCG remains a significant risk factor for adverse outcomes. Previous studies by Jareemit et al. similarly demonstrated that higher initial  $\beta$ -hCG correlates with increased chemotherapy requirement and relapse risk [21]. Logistic regression identified several independent predictors of persistent disease. Age >30 years showed an odds ratio (OR) of 1.17 (95% CI: 1.02-16.35, p=0.03), indicating a modest but significant risk increase. High baseline  $\beta$ -hCG (>10<sup>5</sup> mIU/mL) had OR 3.92 (95% CI: 1.71-8.97, p=0.001), confirming its strong prognostic role. Plateau/rising  $\beta$ -hCG trend was the most powerful predictor with OR 5.64 (95% CI: 2.10-12.80, p=0.001), emphasizing its clinical importance in monitoring disease progression [22]. High FIGO risk score demonstrated OR 4.21 (95% CI: 1.58-10.92, p=0.002), and presence of metastasis showed OR 6.78 (95% CI: 1.44-32.60, p=0.003), both indicating significantly higher likelihood of persistent disease. These findings are consistent with FIGO risk stratification models, which emphasize that metastatic spread and high-risk scoring are major determinants of treatment resistance and prognosis [23].

**LIMITATIONS**

This study has several limitations. It was conducted in a single tertiary care center with a relatively small sample size of 50

patients, which may limit generalizability. The cross-sectional design restricts long-term follow-up assessment of recurrence and survival outcomes. Serial  $\beta$ -hCG monitoring intervals were not fully standardized in all cases, potentially introducing variability in trend interpretation. In addition, potential confounding factors such as treatment regimen heterogeneity and patient adherence were not fully controlled, which may influence outcome assessment.

## CONCLUSION

Serum  $\beta$ -hCG trend analysis is a powerful and reliable tool for predicting clinical outcomes in patients with persistent gestational trophoblastic neoplasia. In this study, a declining  $\beta$ -hCG pattern was strongly associated with complete remission (100%), whereas plateau or rising trends were significantly linked with persistent disease (66.67%) and recurrence (33.33%). High FIGO risk score (OR 4.21, 95% CI: 1.58–10.92), presence of metastasis (OR 6.78, 95% CI: 1.44–32.60), and abnormal  $\beta$ -hCG kinetics (OR 5.64, 95% CI: 2.10–12.80) were significant predictors of poor prognosis. These findings highlight that serial  $\beta$ -hCG monitoring not only reflects treatment response but also provides early prognostic stratification, enabling timely therapeutic modification. Incorporating strict  $\beta$ -hCG surveillance into clinical practice can improve remission rates, reduce recurrence risk, and enhance overall survival outcomes in PGTN patients.

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## CONFLICT OF INTEREST

None declared

## ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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