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Socio-Demographic and Clinical Characteristics of Patients with Persistent Gestational Trophoblastic Neoplasia

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Abstract

Background: *Gestational Trophoblastic Disease (GTD) encompasses a range of disorders resulting from abnormal placental trophoblast cell growth, which can be either benign or malignant. This study aims to examine the socio-demographic and clinical factors associated with the risk of persistent GTN.*

Aim of the Study: *The aim of the study was to evaluate the socio-demographic and clinical characteristics associated with patients diagnosed with persistent Gestational Trophoblastic Neoplasia.*

Methods: *This cross-sectional study was conducted at the Gynecological Oncology Outpatient Department of BSMMU, Dhaka, during 2021, and involved 50 patients diagnosed with molar pregnancy through histopathological confirmation. Data analysis was performed using SPSS version 20, employing chi-square tests and logistic regression analysis. A significance level of $p<0.05$ was used to determine statistical relevance.*

Result: *Patients with GTN were notably younger, with 71.4% being under 20 years old. They had lower socioeconomic status, as 85.7% earned less than 6000 Tk, and were primarily underweight (100%). All GTN-positive patients experienced the expulsion of grape-like vesicles and exhibited thyrotoxic symptoms (85.7%). A history of molar pregnancy was present in 71.4% of the cases, and 71.4% had theca lutein cysts, with 57.1% of these cysts being larger than 6 cm. Multivariate analysis identified age as a significant predictor of GTN (OR: 1.17, $p = 0.030$).*

Conclusion: *Younger age, lower income, and specific ultrasound findings, such as cystic vesicles and large theca lutein cysts, are significant risk factors for persistent Gestational Trophoblastic Neoplasia, highlighting the importance of early detection and risk stratification.*

Keywords: *Gestational Trophoblastic Neoplasia, Socio-Demographic Factors, Clinical Characteristics, Risk Factors, Multivariate Analysis*

1. Introduction

Gestational Trophoblastic Disease (GTD) encompasses a spectrum of disorders originating from the abnormal proliferation of trophoblastic cells within the placenta.[1] These conditions can be categorized into benign forms, such as complete and partial hydatidiform moles, and malignant forms, including invasive moles, placental-site trophoblastic tumors (PSTT), and choriocarcinoma.[2,3]

Abnormal fertilization events, such as those occurring during ectopic pregnancies, abortions, or term and preterm pregnancies, are strongly associated with the development of these lesions.[4] Hydatidiform moles, which constitute approximately 80% of GTD cases, are

characterized by the presence of multiple vesicular formations that enlarge the uterus and are considered precursors to malignant conditions.[5,6,7,8] Malignant forms of GTD, collectively termed gestational trophoblastic neoplasia (GTN), include rare but aggressive conditions such as invasive moles and choriocarcinoma. While these neoplasms exhibit significant potential for metastasis, they are typically highly responsive to treatment, underscoring the importance of timely diagnosis and intervention.[2,3]

Persistent Gestational Trophoblastic Neoplasia (PGTN) represents a complex subset of GTN that requires extended follow-up and tailored treatment approaches. Among the malignant forms, choriocarcinoma is particularly aggressive, with an estimated incidence of 1 in 40,000–50,000 pregnancies and a prevalence of 1 in 40 cases of hydatidiform mole.[9,10] Despite its severity, the majority of patients with choriocarcinoma achieve favorable outcomes due to the tumor's responsiveness to chemotherapy and the availability of reliable markers like human chorionic gonadotropin (hCG) for monitoring disease progression. [11,12] Accurate and consistent measurement of hCG levels remains pivotal for diagnosing and tracking PGTN. Recognizing this, the International Federation of Gynecology and Obstetrics (FIGO) has standardized terminology by promoting the use of "gestational trophoblastic neoplasia" (GTN) over older classifications, reinforcing the need for precise diagnosis and optimal management strategies. [13]

The socio-demographic and clinical characteristics of patients play a crucial role in identifying risk factors for GTN and guiding effective management. For example, ovarian molar pregnancies—rare events linked to abnormal fertilization—highlight the complexity of GTD, occurring in 1 in 7,000 to 1 in 40,000 live births.[14] In resource-rich countries, advancements such as routine ultrasound have substantially reduced delays in GTN diagnosis. However, in developing regions, late presentations and diverse clinical symptoms are still prevalent, reflecting disparities in healthcare access and early detection.[15,16] Following the evacuation of a molar pregnancy, monitoring β-hCG levels has become a cornerstone of care, often sufficient to detect disease progression without the need for prophylactic chemotherapy.[17]

Despite significant advances in chemotherapy-based treatment, gaps in GTN management persist, particularly regarding fertility preservation and the risk of recurrent molar pregnancies. Some studies suggest that expectant management involving close β-hCG monitoring after surgical evacuation can achieve remission in select cases, potentially avoiding the need for immediate chemotherapy.[18,19,20] While chemotherapy ensures high cure rates, its implications for reproductive health and long-term outcomes warrant further research. To address these gaps, our study focuses on evaluating socio-demographic and clinical factors influencing the risk of persistent GTN, aiming to improve understanding and inform better management strategies for this condition.

2. OBJECTIVE

- The aim of the study was to evaluate the socio-demographic and clinical characteristics associated with patients diagnosed with persistent Gestational Trophoblastic Neoplasia.

3. METHODOLOGY & MATERIALS

This cross-sectional study was carried out at the Gynecological Oncology Outpatient Department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from January to December 2021. The study included 50 participants diagnosed with molar pregnancy based on histopathological confirmation.

Inclusion Criteria

- Patients with a histopathologically confirmed diagnosis of molar pregnancy.

Exclusion Criteria

- Individuals with diagnosed abortions, such as missed or incomplete abortions.
- Patients with a prior hysterectomy performed due to molar pregnancy.
- Those who declined to participate in the study.

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

The study received approval from the Institutional Review Board (IRB) of BSMMU. Data analysis was performed using SPSS version 20, with continuous variables summarized as means with standard deviations and categorical variables as frequencies and percentages. 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 of less than 0.05 was considered statistically significant.

4. RESULTS

Table 1. *Association of GTN Status with Age (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[s]
Range (min-max)	18-42	18-44	

Table 1 shows that nearly three-fourths of the GTN-positive subjects, 5 (71.4%), were under the age of 20, compared to 7 (16.3%) in the GTN-negative group. The mean age was 25 ± 11.28 years in the GTN-positive group and 34.28 ± 9.59 years in the GTN-negative group. The difference in age between the two groups was statistically significant ($p < 0.05$).

Table 2. *Association of GTN Status with Monthly Income (n=50)*

Monthly Income (Tk)	GTN Positive (n=7)	GTN Negative (n=43)	p-value
<6000	6 (85.7%)	13 (30.2%)	0.038[s]
6001-15000	1 (14.3%)	9 (20.9%)	
15001-30000	0 (0.0%)	13 (30.2%)	
>30000	0 (0.0%)	8 (18.7%)	

Table 2 reveals that the majority of GTN-positive subjects, 6 (85.7%), had a monthly income of less than 6000 Tk, compared to 18 (41.9%) in the GTN-negative group. The difference in monthly income between the two groups was statistically significant ($p < 0.05$).

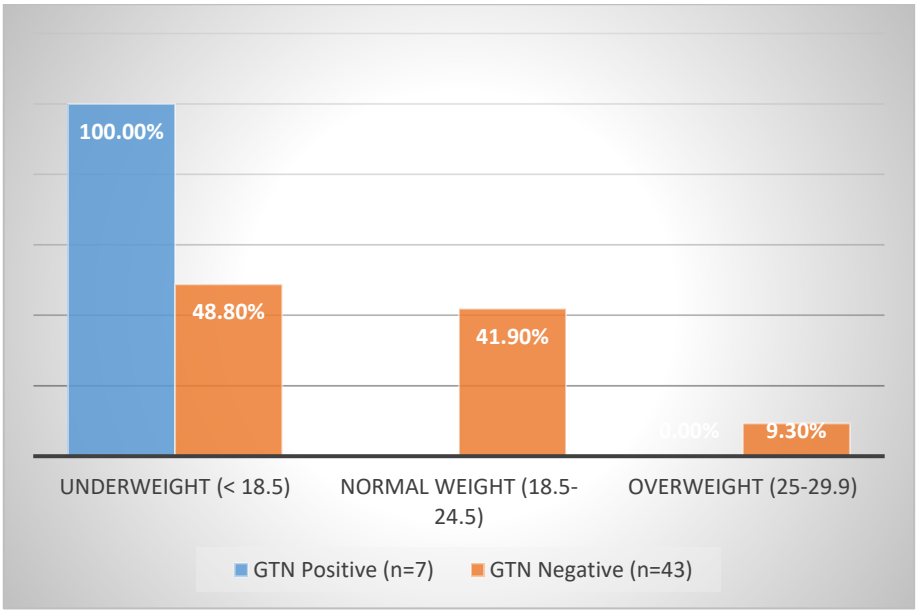

Figure 1. *Association of GTN Status with body mass index (n=50)*

Figure 1 shows that all GTN-positive patients, 7 (100.0%), were underweight, compared to 21 (48.8%) in the GTN-negative group. The difference in body mass index between the two groups was statistically significant ($p < 0.05$).

Table 3. *Distribution of Study Subjects by Presenting Symptoms (n=50)*

Presenting Symptom		GTN Positive (n=7)		GTN Negative (n=43)	
		n	%	N	%
Duration of PV bleeding	0-2 Weeks	6	85.7	43	100.0
	>6 months	1	14.3	0	0.0
Lower abdominal pain	Present	6	85.7	41	95.3
H/O Abortion	Present	0	0.0	17	39.5
H/O Expulsion of grape like vesicle	Yes	7	100.0	26	60.5
	No	0	0.0	17	39.5
Size of the vesicle	>1cm	0	0.0	33	76.7
	>2cm	7	100.0	10	23.3
Gestational age	0-8 weeks	2	28.5	20	46.5
	8-12 weeks	4	57.1	22	51.1
	>12 weeks	1	14.2	1	2.3
H/O Thyrotoxic feature	Present	6	85.7	11	25.6
H/O mole in previous pregnancy	Present	5	71.4	9	20.9
Family history of molar pregnancy	Molar pregnancy	4	57.1	0	0.0
	Choriocarcinoma	1	14.3	0	0.0
	No	2	28.6	43	100.0

It was observed that the majority, 6 (85.7%), of GTN-positive patients had PV bleeding for a duration of 2 weeks, compared to 43 (100.0%) in the GTN-negative group. Lower abdominal pain was present in 6 (85.7%) of GTN-positive cases and 43 (100.0%) of GTN-negative cases. A history of abortion was absent in all 7 (100.0%) GTN-positive cases. A history of expulsion of grape-like vesicles was found in 7 (100.0%) GTN-positive cases and 26 (60.5%) GTN-negative cases, respectively. All 7 (100.0%) GTN-positive patients had vesicle sizes >2 cm. The gestational age of patients was between 8–12 weeks in 4 (57.1%) GTN-positive cases and 22 (51.1%) GTN-negative cases.

Almost three-fourths, 5 (71.4%), of GTN-positive patients had a history of mole in previous pregnancies, compared to 9 (20.9%) in the GTN-negative group. Thyrotoxic features were observed in 6 (85.7%) of GTN-positive cases and 11 (25.6%) of GTN-negative cases. Additionally, a family history of molar pregnancy was noted in 4 (57.1%) of GTN-positive patients.

Table 4. *Association of GTN Status with Parity (n=50)*

Parity	GTN Positive (n=7)		GTN Negative (n=43)		*p* value
	n	%	n	%	
0	3	42.9	8	18.6	0.049[s]
1-3	0	0	21	48.8	
>3	4	57.1	14	32.6	

Table 4 shows that more than half, 4 (57.1%), 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 ($p < 0.05$).

Table 5. *Association of USG Findings with GTN Status (n=50)*

USG investigation		GTN Positive (n=7)		GTN Negative (n=43)		*p* value
		n	%	n	%	
USG of uterus	Vesicular	3	42.8	23	53.5	0.005[s]
	Cystic	2	28.6	18	41.8	
	Snow storm appearance	0	0.0	2	4.7	
	Necrotic	2	28.6	0	0.0	
USG of ovary	Normal	2	28.6	27	62.8	0.088[ns]
	Theca lutein cyst	5	71.4	16	37.2	
Size of theca lutein cyst	<6 cm	1	14.3	9	20.9	0.029[s]
	>6 cm	4	57.1	6	14.0	
	No cyst	2	28.6	28	65.1	

Table 5 shows that most of the GTN-positive patients, 5 (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 6. *Association of GTN Status with Other Investigations (n=50)*

Investigations		GTN Positive (n=7)		GTN Negative (n=43)		*p* value
		n	%	n	%	
Histopathology report	Molar pregnancy	6	85.7	43	100.0	0.012[s]
	Choriocarcinoma	1	14.3	0	0.0	
Xray Chest	Normal	5	71.4	43	100.0	0.001[s]
	Canon ball appearance	2	28.6	0	0.0	
CT scan of chest	Normal	3	42.9	3	7.0	0.001[s]
	Cannon ball	1	14.3	0	0.0	
	Not done	3	42.9	40	93.0	

It is observed that the majority, 6 (85.7%), of patients in the GTN positive group had molar pregnancy in the histopathology report, whereas 43 (100%) were found in the GTN negative group. X-ray chest showed a cannonball appearance in 2 (28.6%) of GTN positive cases. CT scan of the chest showed a cannonball appearance in 1 (14.3%) of GTN positive cases. The differences in histopathology reports, X-ray chest findings, and CT scan chest results were statistically significant ($P<0.05$) between the GTN positive and GTN negative groups.

Table 7. *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	0.030[s]	1.17	1.02	16.35
H/O mole in previous pregnancy	2.01	1.57	0.199[ns]	0.48	0.35	1.93
Thyrotoxic feature	1.39	1.53	0.363[ns]	0.03	0.2	1.05
Uterus size per abdomen	2.56	1.64	0.119 [ns]	0.88	0.52	2.94

Table 7 shows the results of the multivariate logistic regression model, with the odds ratio (OR) adjusted for covariates. The 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 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.

5. Discussion

This study investigates the socio-demographic and clinical characteristics associated with persistent gestational trophoblastic neoplasia (PGTN) among patients at a tertiary care hospital. PGTN, a complication following molar pregnancies, poses significant risks to maternal health and requires prompt diagnosis and management. Our findings highlight the multifactorial nature of the condition, with factors such as younger age, lower income, underweight status, and a history of molar pregnancies playing pivotal roles. The presence of specific clinical and ultrasound characteristics further emphasizes the importance of early detection and targeted interventions to improve patient outcomes.

Our 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,[21] which also identified younger age as a significant risk factor for Gestational Trophoblastic Disease (GTD), underscoring the importance of age in GTN development and persistence.

Our study found that the majority of GTN-positive patients (85.7%) had a monthly income of less than 6000 Tk, significantly higher than the 41.9% observed in the GTN-negative group ($p < 0.05$). This aligns with the findings of Capobianco et al.[21] in their study, which also identified lower income as a significant risk factor for Gestational Trophoblastic Disease (GTD). The similarity between our results and those of Capobianco et al. highlights the critical role of socio-economic factors, particularly income, in the development and persistence of GTN.

In our study, all GTN-positive patients were underweight, in contrast to a smaller proportion in the GTN-negative group. This significant difference in body mass index suggests that underweight status may be associated with an increased likelihood of persistent GTN, highlighting the importance of monitoring nutritional status in these patients for potential interventions.

In our study, several clinical features were more prevalent in GTN-positive patients compared to the GTN-negative group. The majority of GTN-positive patients had prolonged PV bleeding (85.7%) and experienced lower abdominal pain (85.7%). Notably, all GTN-positive patients had a history of expulsion of grape-like vesicles, with all presenting with vesicle sizes greater than 2 cm. A history of previous molar pregnancy was also significantly higher in the GTN-positive group (71.4%), and thyrotoxic features were more common (85.7%). Additionally, a family history of molar pregnancy was found in over half of the GTN-positive patients, underscoring the role of these clinical features in identifying individuals at higher risk for GTN.

More than half of the subjects, 4 (57.1%), in 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.[22] Another study showed that hydatidiform mole was associated with multiparity in 60% of cases.[23]

Ultrasound examination was helpful in making a pre-evacuation diagnosis of molar pregnancy, but the definitive diagnosis was made through histological examination of the products of conception. The use of ultrasound in early pregnancy has likely led to the earlier diagnosis of molar pregnancy.

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 ($p = 0.005$). [24]

The majority, 5 (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.[25]

Histopathology revealed that the majority, 6 (85.7%) in the PGTN-positive group and 43 (100.0%) in the PGTN-negative group, showed molar pregnancy. Chest X-ray showed a cannonball appearance in 2 (28.6%) of the PGTN-positive group. Chest CT scan revealed a cannonball appearance in 1 (14.3%) of the PGTN-positive cases. All of these investigations were significantly associated with the development of persistent PGTN ($p = 0.012$, $p = 0.001$, $p = 0.001$).

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.[26] 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, $p = 0.004$).[27] Additionally, histopathologic features, uterine size, lutein cysts >6 cm, and pre-evacuation β-hCG levels were predictors of persistent gestational trophoblastic neoplasia.[28]

6. Limitations of the Study

This study had several limitations:

- Being conducted at a single tertiary care hospital in Dhaka, the results may not be generalizable to a broader population.
- The short duration of the study, constrained by the investigator's studentship status,

impacted the resources available for data collection and analysis.

- The small sample size reduces statistical power and limits the ability to extrapolate the findings to larger populations.
- As a cross-sectional study without a comparison group, the identified risk factors for persistent disease should be validated in future longitudinal or analytic observational studies for more robust conclusions.

7. Conclusion

This study examined the socio-demographic and clinical factors associated with persistent Gestational Trophoblastic Neoplasia (GTN). It found that younger age, particularly under 20 years, and a lower monthly income were significantly linked to GTN. Additionally, a history of expulsion of grape-like vesicles and thyrotoxic features was more common in GTN-positive patients. Ultrasound findings, such as large theca lutein cysts, were also key indicators of GTN. The analysis confirmed that younger age increased the risk for developing persistent GTN. These findings emphasize the importance of early detection and risk assessment for patients at risk of GTN.

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