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**Original Research Article**

# Treatment modalities and clinical outcomes in patients with gestational trophoblastic disease

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## ABSTRACT

**Background:** Gestational trophoblastic disease (GTD) encompasses a diverse group of disorders characterized by abnormal trophoblastic tissue proliferation, including premalignant conditions like hydatidiform moles and malignant types such as choriocarcinoma and persistent trophoblastic disease, which carry significant malignant potential. The purpose of this study was to evaluate the effectiveness of various treatment modalities and the clinical outcomes in patients diagnosed with gestational trophoblastic disease. The aim of the study was to evaluate the effectiveness of various treatment modalities and the clinical outcomes in patients diagnosed with gestational trophoblastic disease.
**Methods:** This descriptive cross-sectional study, conducted at the Department of Obstetrics and Gynaecology, Sir Salimullah Medical College and Mitford Hospital, Dhaka (November 2012 - November 2013), included 50 cases of gestational trophoblastic disease (GTD). Inclusion criteria were fresh, incompletely treated, and recurrent GTD cases. Data were collected via a pretested questionnaire, analyzed using SPSS, and presented as descriptive statistics. Ethical approval and informed consent were obtained from all participants.
**Results:** Among 50 GTD cases, 60% were complete moles, with 94.44% of persistent disease linked to prior molar pregnancies. P/V bleeding was the most common symptom. Choriocarcinoma showed 50% metastasis, mainly to lungs, and 86% remission with EMACO therapy. Suction evacuation treated 56% of molar pregnancies, with 13.5% progressing to persistent mole and 4.5% to choriocarcinoma.
**Conclusions:** This study highlights the importance of early detection, timely treatment, and regular follow-up in improving outcomes for patients with gestational trophoblastic disease.

**Keywords:** Clinical outcomes, Choriocarcinoma, Gestational trophoblastic disease, Molar pregnancy

## INTRODUCTION

Gestational trophoblastic disease (GTD) encompasses a diverse group of disorders marked by abnormal trophoblastic tissue proliferation. These include premalignant forms such as partial hydatidiform mole (PHM) and complete hydatidiform mole (CHM), alongside malignant types like invasive mole, choriocarcinoma, placental-site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT). Hydatidiform mole is the most prevalent subtype, with an incidence of 0.5-3.0 per 1,000 pregnancies in Europe, while GTD is observed more frequently in Asia, potentially due to genetic, dietary, or data reporting factors.[1-5] Although rare, GTD is clinically significant due to its malignant potential. Advances in chemotherapy and the utilization of sensitive tumor markers such as human chorionic gonadotropin (hCG) have shifted GTD from

being one of the most fatal malignancies to one of the most treatable conditions.[6]

Gestational trophoblastic disease (GTD) typically presents with symptoms such as vaginal bleeding, uterine enlargement, and elevated hCG levels, which facilitate early detection.[7,8] Diagnosis is achieved through a combination of clinical evaluation, imaging studies, and biochemical markers, with hCG serving as a pivotal tool for diagnosis, management, and ongoing monitoring. Preoperative evaluations, including metastatic screening, chest X-rays, serum hCG measurement, and comprehensive blood tests, are crucial for accurate staging and preparation. Tailored treatment plans based on pathology and risk assessment have led to significantly improved outcomes, underscoring the critical role of early and accurate diagnosis in the effective management of GTD.[9]

The management of gestational trophoblastic disease (GTD) has advanced considerably, particularly with the introduction of chemotherapy, which has rendered low-risk gestational trophoblastic neoplasia (GTN) highly treatable. Single-agent chemotherapy using methotrexate (MTX) or actinomycin D (ActD) is the standard treatment for most low-risk GTN cases, achieving remission rates of 50% to 90% depending on the chosen regimen and patient characteristics.[10,11] For patients resistant to initial treatments, second or third-line therapies often result in remission, contributing to an overall survival rate nearing 100%.[12-14] To enhance care, the European Organisation for Treatment of Trophoblastic Diseases (EOTTD) has established standardized guidelines aimed at improving diagnosis, management, and follow-up for GTD patients across Europe, addressing disparities in healthcare access and practices.[15]

Despite significant advancements, challenges in the management of GTD persist. Persistent or recurrent disease, resistance to treatment, and issues with patient compliance remain major obstacles. Additionally, certain subtypes, such as placental-site trophoblastic tumour (PSTT) and epithelioid trophoblastic tumour (ETT), pose unique challenges due to their distinct biological characteristics,[9] including slower progression, lower hCG production, and decreased sensitivity to chemotherapy, complicating treatment strategies. The rarity of GTD further limits robust evidence from randomized controlled trials, leading to variability in treatment protocols that may impact patient outcomes.[15] Variations in healthcare infrastructure and access, particularly across Europe, highlight the critical need for unified guidelines, such as those developed by the EOTTD, to standardize care and ensure equitable treatment for all patients.

Gestational Trophoblastic Disease (GTD) represents a rare yet highly curable group of disorders, with advancements in chemotherapy and improved diagnostic techniques significantly enhancing patient outcomes. However, challenges such as resistance to treatment, recurrence, and variations in clinical management across populations continue to impede optimal care. Furthermore, limited evidence from randomised trials and inconsistencies in treatment protocols highlight the need for comprehensive evaluations of therapeutic strategies. The purpose of this study was to assess the effectiveness of various treatment modalities and the clinical outcomes in patients diagnosed with gestational trophoblastic disease.

## METHODS

This descriptive cross-sectional study was conducted at the Department of Obstetrics and Gynaecology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, from November 2012 to November 2013. The study included all cases of gestational trophoblastic disease (GTD) admitted to SSMC & MH, Dhaka, during the study period, with a minimum sample size of 50 cases.

### *Inclusion criteria*

Inclusion criteria were the fresh cases of GTD (hydatidiform mole, invasive mole, choriocarcinoma, and PSTT) presenting for the first time for treatment, previously incompletely treated cases of GTD and recurrent cases of GTD.

### *Exclusion criteria*

Patients with known other types of gynecological malignancies, patients with severe unrelated chronic illnesses that could interfere with the study outcomes were excluded.

Informed consent was obtained from all participants, ensuring confidentiality and voluntary participation. Data were collected using a structured questionnaire, developed based on the research questions, objectives, and study variables. The questionnaire was pretested among 15 patients for clarity, accuracy, and validity, with minor modifications made before final use. Patient history and clinical examinations were conducted thoroughly. Data collection occurred over one year, with a target minimum sample size of 50. Each patient's history and examination were completed within one hour. Patients were monitored during their hospital stay and followed up for one year to diagnose and treat cases of persistent trophoblastic disease. Data were checked, verified for consistency, and edited for final analysis. After coding, data were entered into a computer using SSPS/PC software. Data validation, cleaning, and analysis were performed using SSPS/PC software, with results presented as means, medians, modes, standard deviations, and percentages. Findings were displayed in tables, pie charts, and graphs using MS Excel. A work manual and standard case record form were created and pretested to ensure high-quality data collection. The pretest ensured respondents understood the questionnaire and could answer accordingly. The study was approved by the ethical committee of Sir Salimullah Medical College & Mitford Hospital, Dhaka. Participants

were informed of their right to decline participation or any question and assured that their information would be used solely for research purposes.

## RESULTS

Among the 50 cases of GTD, 30 cases (60.00%) were diagnosed as complete mole, 2 cases (4.00%) as partial mole, 10 cases (20.00%) as persistent trophoblastic disease, and 8 cases (16.00%) as choriocarcinoma. Of the 18 patients diagnosed at admission with persistent trophoblastic disease and choriocarcinoma, 17 cases (94.44%) had a history of antecedent molar pregnancy, while 1 case (5.56%) had a history of normal delivery (Table 1).

Among patients with molar pregnancy (n=32), the most common presenting symptom was P/V bleeding, observed in 18 cases (56%), followed by P/V bleeding with passage of vesicles in 7 cases (22%) and P/V bleeding with lower abdominal pain in 2 cases (6%). Amenorrhea was reported in 5 patients (16%), with 4 cases (13%) associated with exaggerated pregnancy symptoms and 1 case (3%) with preeclampsia. Among patients with persistent mole and choriocarcinoma (n=18), P/V bleeding with lower abdominal pain was the most frequent symptom, reported in 9 cases (50%). Amenorrhea with lower abdominal pain occurred in 5 cases (28%), while amenorrhea with breathlessness was noted in 2 cases (11%). P/V bleeding with neurological features and vaginal nodules was present in 2 cases (11%) (Table 2).

**Table 1: Distribution of GTD types and antecedent pregnancy in persistent trophoblastic disease and choriocarcinoma.**

| Variable | | No. of cases (N) | Percentage (%) |
|---|---|---|---|
| **Type of GTD** | Complete mole | 30 | 60.00 |
| | Partial mole | 2 | 4.00 |
| | Persistent trophoblastic disease | 10 | 20.00 |
| | Choriocarcinoma | 8 | 16.00 |
| **Type of antecedent pregnancy** | Molar pregnancy | 17 | 94.44 |
| | Normal delivery | 1 | 5.56 |

**Table 2: Clinical presentation of patients with molar pregnancy, persistent mole, and choriocarcinoma.**

| GTD type | Presenting symptoms | No. of cases (N) | Percentage (%) |
|---|---|---|---|
| **Molar pregnancy** | P/V bleeding | 18 | 56.00 |
| | P/V bleeding with lower abdominal pain | 2 | 6.00 |
| | P/V bleeding with passage of vesicles | 7 | 22.00 |
| | Amenorrhoea with exaggerated pregnancy symptoms | 4 | 13.00 |
| | Amenorrhoea with preeclampsia | 1 | 3.00 |
| **Persistent mole and choriocarcinoma** | P/V bleeding with lower abdominal pain | 9 | 50.00 |
| | Amenorrhoea with lower abdominal pain | 5 | 28.00 |
| | Amenorrhoea with breathlessness | 2 | 11.00 |
| | P/V bleeding with neurological feature | 1 | 5.50 |
| | P/V bleeding with vaginal nodule | 1 | 5.50 |

**Table 3: Metastases, follow-up outcomes in choriocarcinoma.**

| Variable | | No. of cases (N) |
|---|---|---|
| **Metastases of choriocarcinoma** | Total cases of choriocarcinoma | 8 |
| | Metastasis present | 4 |
| | Metastasis in lungs | 2 |
| | Metastasis in vagina | 1 |
| | Metastasis in central nervous system | 1 |

Among the 8 cases of choriocarcinoma, 4 presented with metastasis, including 2 cases (50%) with metastasis to the lungs, 1 case (25%) to the vagina, and 1 case (25%) to the central nervous system (Table 3).

Among the 4 patients with molar pregnancy who had theca lutein cysts, 2 patients (50%) developed a persistent mole, 1 patient (25%) developed choriocarcinoma, and 1 patient (25%) was cured. All 2 patients with persistent moles were successfully treated and cured using single-agent chemotherapy. Among the patients with choriocarcinoma, 1 patient achieved remission with EMACO therapy, while 1 patient expired during the surveillance period (Table 4).

Out of 32 patients with molar pregnancy, 22 (69%) attended follow-up; of these, 18 (82%) achieved normal β-hCG levels within 6 to 8 weeks, while 3 (13.5%) developed persistent mole, and 1 (4.5%) developed

choriocarcinoma. Among 10 patients with persistent mole, 8 (80%) attended regular follow-up, and all were successfully cured with single-agent chemotherapy. Of these patients in choriocarcinoma, 7 attended follow-up, with 6 (86%) achieving remission through EMACO therapy, while 1 patient (14%) expired during chemotherapy (Table 5).

**Table 4: Fates of patients with theca lutein cyst during follow-up.**

| Type of GTD | No. of patients | Fate |
|---|---|---|
| **Molar pregnancy** | 4 | Persistent mole: 2 |
| | | Choriocarcinoma: 1 |
| | | Cured: 1 |
| **Persistent mole** | 2 | Cured: 2 |
| **Choriocarcinoma** | 2 | Cured: 1 |
| | | Expired: 1 |

**Table 5: Follow-up and outcomes in gestational trophoblastic disease.**

| Variable | | No. of cases (N) |
|---|---|---|
| **Follow-up outcomes in molar pregnancy** | Total patients with molar pregnancy | 32 |
| | Patients who appeared for follow-up | 22 |
| | Patients who failed to follow up | 10 |
| | Patients in remission | 18 |
| | Persistent mole during follow-up | 3 |
| | Choriocarcinoma during follow-up | 1 |
| **Follow-up outcomes in persistent mole** | Total patients with persistent mole | 10 |
| | Patients who appeared for follow-up | 8 |
| | Patients who failed to follow up | 2 |
| **Follow-up outcomes in choriocarcinoma** | Total patients who were supposed to follow-up | 8 |
| | Patients who appeared for follow-up | 7 |
| | Patients who failed to follow up | 1 |
| | Patients in remission (cured with EMACO therapy) | 6 |
| | Patients who died during the course of therapy | 1 |

**Table 6: Treatment modalities in various GTD (n=50).**

| Type of GTD | Treatment received by the patients | No. of cases | Percentage (%) |
|---|---|---|---|
| **Molar pregnancy** | Only suction evacuation | 28 | 56.00 |
| | Suction evacuation followed by chemotherapy | 3 | 6.00 |
| | Suction evacuation followed by total abdominal hysterectomy | 1 | 2.00 |
| **Persistent mole and choriocarcinoma** | Only chemotherapy | 14 | 28.00 |
| | Chemotherapy followed by total abdominal hysterectomy | 2 | 4.00 |
| | Chemotherapy followed by radiation | 2 | 4.00 |
| | | 50 | 100.00 |

All 32 molar pregnancy cases were treated with suction evacuation. Three patients required single-agent chemotherapy due to high risk, and 1 underwent abdominal hysterectomy for uterine perforation. Persistent trophoblastic disease cases were treated with single-agent chemotherapy, while choriocarcinoma cases required multiple-agent chemotherapy (EMACO therapy). Two patients required total abdominal hysterectomy due to uncontrollable hemorrhage, and 2 required chemotherapy followed by radiation for cerebral metastasis (Table 6).

## DISCUSSION

Gestational trophoblastic disease (GTD) is a notable clinical concern in Bangladesh, with its incidence being relatively high, reflecting the need for improved diagnostic and treatment strategies. The condition encompasses a spectrum of trophoblastic disorders, including molar pregnancies, persistent trophoblastic disease, and choriocarcinoma, with lung metastases being common in advanced cases. Early detection through β-hCG monitoring and individualized care has been pivotal in

achieving high remission rates. In this retrospective study, 50 patients with GTD were evaluated at a tertiary hospital in Dhaka. Patients with molar pregnancies were primarily managed with suction evacuation, while those with persistent or metastatic disease received chemotherapy, predominantly the EMACO regimen. The study highlights the importance of early diagnosis, tailored treatment approaches, and consistent follow-up to improve outcomes for GTD patients.

In this study, 60.00% of the GTD cases were diagnosed as complete mole, 4.00% as partial mole, 20.00% as persistent trophoblastic disease, and 16.00% as choriocarcinoma. Of the 18 patients diagnosed at admission with persistent trophoblastic disease and choriocarcinoma, 94.44% had a history of antecedent molar pregnancy. These findings align with those reported by Al et al, where complete mole was the most common type at 43.8% and partial mole at 54.7%.[16] Both studies underscore the significant proportion of patients requiring chemotherapy, highlighting the importance of early diagnosis and tailored treatment strategies for GTD. This consistency across different populations and healthcare settings emphasizes the shared epidemiological and clinical characteristics of GTD.

In our study, the most common presenting symptom among patients with molar pregnancy was P/V bleeding (56%), followed by P/V bleeding with the passage of vesicles (22%) and P/V bleeding with lower abdominal pain (6%). These findings are consistent with the study by Mdoe et al, which also highlighted significant occurrences of these clinical presentations in women with GTD.[17] In their study, partial hydatidiform mole was the most frequent diagnosis (42.9%), followed by complete mole (40.5%), aligning with our observations. Both studies also reported significant associations between elevated hCG levels and GTD. This consistency across different populations emphasizes the importance of recognizing these patterns for timely diagnosis and management.

In our study, among the 8 cases of choriocarcinoma, 4 presented with metastasis, including 2 cases (50%) to the lungs, 1 case (25%) to the vagina, and 1 case (25%) to the central nervous system. Of these patients, 7 attended follow-up, with 6 (86%) achieving remission through EMACO therapy, while 1 patient (14%) expired during chemotherapy. These findings are consistent with the study by Shahzadi et al, which also reported a high remission rate with EMACO therapy for choriocarcinoma, emphasizing its effectiveness.[18] They found that multi-agent chemotherapy, including EMA-CO, led to complete remission in 93% of high-risk GTN patients, similar to our observed success rate. This alignment underscores the efficacy of EMACO therapy in managing metastatic choriocarcinoma and highlights the importance of diligent follow-up to ensure successful outcomes.

Our study revealed that among the four patients with molar pregnancy and theca lutein cysts, 50% developed persistent mole, 25% progressed to choriocarcinoma, and 25% were cured. Among 32 patients with molar pregnancy, 69% attended follow-up, with 82% achieving normal β-hCG levels within 6 to 8 weeks. However, 13.5% developed persistent mole, and 4.5% progressed to choriocarcinoma. 80% of the patients with persistent mole attended regular follow-up, and all were successfully cured with single-agent chemotherapy. Additionally, 1 patient became negative following EMACO therapy during the surveillance period. These results underscore the critical importance of diligent follow-up and highlight the effectiveness of chemotherapy in treating persistent mole while also pointing to the potential risks of progression to more severe conditions.

In our study, all 32 cases of molar pregnancy were treated with suction evacuation, three high-risk patients required single-agent chemotherapy, and one underwent abdominal hysterectomy due to uterine perforation, consistent with the standard approaches described by Ngan et al, persistent trophoblastic disease was managed with single-agent chemotherapy, while choriocarcinoma required multi-agent chemotherapy (EMACO therapy).[19] Additionally, two cases required total abdominal hysterectomy due to uncontrollable hemorrhage, and two needed chemotherapies followed by radiation for cerebral metastasis, aligning with Ngan et al.'s guidelines. These parallels highlight the effectiveness of these treatment protocols.

This study had some limitations. A significant number of patients missed regular follow-ups due to socio-economic challenges, limited education, and lack of health awareness. Essential investigations, such as B-hCG, were not consistently performed due to the unavailability of free testing facilities in government hospitals. The absence of a standardized molar card system hindered proper record-keeping for patients. The small study sample size limits generalizability, and a larger cohort would provide more detailed insights into individual subgroups.

## CONCLUSION

This study evaluated treatment modalities and outcomes in 50 GTD patients. The majority were diagnosed with complete mole (60%), followed by persistent trophoblastic disease (20%) and choriocarcinoma (16%). Molar pregnancies commonly presented with vaginal bleeding, while persistent trophoblastic disease and choriocarcinoma were marked by bleeding and abdominal pain. Choriocarcinoma cases often involved metastasis, with most achieving remission through EMACO chemotherapy. Treatment primarily involved suction evacuation for molar pregnancies, with chemotherapy for persistent trophoblastic disease and choriocarcinoma. Follow-up was critical for successful outcomes, highlighting the need for early detection and consistent monitoring.

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