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Original Research Article

CLINICAL PROFILE OF GESTATIONAL TROPHOBLASTIC DISEASE AT A TERTIARY CARE CENTER

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ABSTRACT

Background: Gestational trophoblastic disease (GTD) comprises disorders caused by abnormal trophoblastic proliferation, with potential progression to gestational trophoblastic neoplasia (GTN). Early diagnosis and risk-based management are crucial for favourable outcomes. This study aimed to describe the clinical profile, treatment approaches, and outcomes of GTD patients managed at a tertiary care centre. **Materials and Methods:** This observational study included 172 GTD patients (2018-2023). Demographic details, clinical features, β-hCG levels, risk classification, treatments, and outcomes were recorded. Patients were categorised as low- or high-risk using WHO/FIGO criteria and managed per institutional protocols. Outcomes assessed included complete response, treatment failure, second-line therapy requirement, and loss to follow-up. **Results:** Most patients were aged 20–30 years (73.3%), with 16.3% aged <20 years. Half were nulliparous (50.6%). Gestational age at presentation was ≤8 weeks in 34.3%, 8–12 weeks in 30.2%, and 13–16 weeks in 32%. Clinical presentation showed 60% symptomatic, mainly bleeding per vaginum (70%). Pre-evacuation β-hCG was >100,000 IU/L in 56%. Low-risk cases comprised 39(85%) and high-risk cases 7(15%). Among low-risk GTN, methotrexate was given to 38(97.4%), with 23 CR, 14 failures, and 1 LFU. Second-line actinomycin-D achieved CR in all 5 patients. EMACO was used in 9 patients, with 8 CR. One patient required EMAEP with CR. In the high-risk group, all seven received EMACO, resulting in six CR and one LFU. **Conclusion:** GTD patients commonly presented early with typical symptoms. Risk-based treatment achieved high remission, with methotrexate effective in low-risk cases and multi-agent chemotherapy benefiting high-risk patients. Timely diagnosis and protocol-driven care resulted in favourable outcomes.

INTRODUCTION

Gestational trophoblastic disease (GTD) encompasses a group of disorders arising from abnormal proliferation of placental trophoblastic tissue.1 These conditions range from benign forms, such as hydatidiform mole, to malignant entities collectively known as gestational trophoblastic neoplasia (GTN), including invasive mole, choriocarcinoma, placental-site trophoblastic tumour and epithelioid trophoblastic tumour.2 GTD remains relatively rare but is clinically significant due to its potential for malignant transformation and ability to metastasise.3

The incidence of molar pregnancies and subsequent GTN varies by region. In high-income countries, the incidence of hydatidiform mole has been estimated at approximately 1 in 600 therapeutic abortions and 1 in 1,000-1,200 pregnancies.4 Risk factors identified include maternal age (particularly extremes of reproductive life) and prior molar pregnancy, among others.5 The ability to diagnose GTD early has improved significantly with advances in transvaginal ultrasound imaging and sensitive assays for β-human chorionic gonadotropin (β-hCG).6

Management of GTD hinges on prompt uterine evacuation of the molar tissue, followed by careful surveillance of β-hCG levels to detect persistent disease.4 In cases where the disease persists or progresses to GTN, classification into low-risk and high-risk categories (for example, using the International Federation of Gynaecology and Obstetrics (FIGO) staging combined with a prognostic scoring system) guides treatment

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strategies.[7,8] Low-risk GTN is usually managed with single-agent chemotherapy (e.g. methotrexate or actinomycin-D). In contrast, high-risk disease requires multi-agent regimens and may include surgery or radiotherapy in select cases.[9]

Despite its malignant potential, GTD and GTN are among the success stories in oncology, with reported cure rates of 80-90% in many specialist centres when managed appropriately.[10] However, in low- and middle-income settings, challenges related to delayed diagnosis, inadequate follow-up, limited facilities, and patient non-compliance may adversely affect outcomes. Therefore, studies conducted in tertiary care centres, especially in resource-constrained environments, play a critical role in understanding local disease patterns, outcomes, and areas that need improvement. Therefore, the present study aimed to assess the types of GTD encountered, demographic and clinical characteristics of affected patients, their management according to risk-stratified protocols, and treatment outcomes in terms of response and follow-up at a tertiary care referral centre.

MATERIALS AND METHODS

This observational study included 172 patients registered and treated for GTD at the Thanjavur medical college and Hospital, between 2018-2023. Ethical approval for the study protocol was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all participants before inclusion.

Inclusion Criteria

All patients diagnosed with GTD, including partial mole, complete mole, and gestational trophoblastic neoplasia, who were registered during the study period, were included. Diagnosis was confirmed using clinical assessment, ultrasonography, and serial serum β-hCG measurements.

Exclusion Criteria

Patients with incomplete medical records, those who were lost to follow-up immediately after diagnosis, and those who did not have adequate β-hCG monitoring data were excluded.

Methodology

Demographic details, such as age and parity, were recorded. The clinical presentation, gestational age at diagnosis, evacuation details, and pre-treatment β-hCG levels were documented. Patients were stratified into low (score < 6) and high-risk (score ≥ 6) groups using the WHO/FIGO risk scoring system.

Management was carried out according to the established GRH treatment protocol, wherein low-risk patients received weekly methotrexate 50 mg with β-hCG levels monitored at two-week intervals, followed by one consolidation dose after normalisation of β-hCG levels. In cases where the methotrexate response failed, second-line therapy with actinomycin-D was initiated, and those who failed second-line treatment were shifted to multi-agent chemotherapy using the EMACO regimen. High-risk patients were started directly on Etoposide, Methotrexate, Actinomycin-D, Cyclophosphamide and Vincristine (EMACO) combination chemotherapy, with β-hCG levels assessed after each cycle and two additional consolidation cycles administered once normalisation was achieved; patients showing resistance to EMACO were managed with alternative regimens such as Etoposide, Methotrexate, Actinomycin-D, Etoposide and Cisplatin (EMAEP), Cisplatin, Etoposide and Bleomycin (PEB), or Cisplatin, Vinblastine and Bleomycin (PVB) according to clinical judgment.

Outcomes assessed included response to first-line therapy, need for second-line or multi-agent chemotherapy, default rates, and treatment completion. A complete response was defined as sustained normalisation of β-hCG values for three consecutive weekly measurements. Treatment failure was recorded when β-hCG values plateaued or increased despite therapy. Patients were monitored for chemotherapy-related toxicity, compliance with follow-up, and overall treatment responses.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS v21.0. Categorical variables are presented as frequencies and percentages.

RESULTS

Most patients were aged 20–30 years (73.3%), with half being nulliparous (50.6%). The majority presented before 16 weeks of gestation, with early gestational age distribution showing 34.3% ≤8 weeks, 30.2% between 8–12 weeks, and 32% between 13–16 weeks. [Table 1]

Table 1: Demographic and clinical characteristics at presentation

Category	Sub-category	N (%)
Age (years)	<20	28 (16.3%)
	20–30	126 (73.3%)
	31–40	14 (8.1%)
	>40	4 (2.3%)
Parity	Nil	87 (50.6%)
	1	56 (32.6%)
	2	20 (11.6%)
	≥3	9 (5.2%)
Gestational age(weeks)	≤8	59 (34.3%)
	8–12	52 (30.2%)
	13–16	55 (32%)
	>16	6 (3.5%)

Most patients were symptomatic (60%), and bleeding per vaginum was the predominant presenting symptom (70%). Hyperemesis (17%) and abdominal pain (14%) were less common, while respiratory distress (1.9%) and neurological symptoms (0.9%) were rare. Risk stratification showed that the majority were in low-risk GTN (85%), 15% in the high-risk category. [Table 2]

Table 2: Clinical presentation, symptom profile and risk stratification

Category	Sub-category	N (%)
Clinical presentation	Asymptomatic (routine USG)	69 (40%)
	Symptomatic	103 (60%)
Symptoms	Bleeding per vaginum	72 (70%)
	Hyperemesis	18 (17%)
	Abdominal pain	15 (14%)
	Respiratory distress	2 (1.9%)
	Neurological symptoms	1 (0.9%)
Risk stratification	Low-risk GTN	39 (85%)
	High-risk GTN	7 (15%)

Pre-evacuation hCG levels were <1,000 in 11 (6%), 1,000–10,000 in 20 (12%), 10,000–100,000 in 45 (26%), and >100,000 in 96 (56%). Pre-treatment hCG levels were <1,000 in 3 (6%), 1,000–10,000 in 12 (26%), 10,000–100,000 in 14 (31%), and >100,000 in 17 (37%). [Table 3]

Table 3: hCG levels before evacuation and before treatment

hCG Range	Pre-Evacuation	Pre-Treatment
< 1,000	11 (6%)	3 (6%)
1,000–10,000	20 (12%)	12 (26%)
10,000–100,000	45 (26%)	14 (31%)
>100,000	96 (56%)	17 (37%)

Among the low-risk group (n=39), methotrexate was given to 38 (97.4%), resulting in 23 complete responses (CR), 14 failures, and 1 lost to follow-up (LFU). Actinomycin D was used in five (12.8%) patients, all of whom achieved CR. EMACO was used in eight (20.5%) patients after Act-D failure, with seven CR and one failure, and was also used directly in 1 (2.6%) patient who achieved CR. EMAEP was required in 1 (2.6%) patient with CR. In the high-risk group (n=7), EMACO was administered to all seven (100%) patients, resulting in 6 CR and 1 LFU. [Table 4]

Table 4: Treatment outcomes in low-risk and high-risk GTN

Group	Treatment	N (%)	Outcome Notes
Low-risk GTN (n=39)	Methotrexate (1st line)	38 (97.4%)	23 CR, 14 failure, 1 LFU
	Actinomycin-D (2nd line)	5 (12.8%)	All 5 CR
	EMACO (after Act-D failure)	8 (20.5%)	7 CR, 1 failure
	EMACO (direct in 1 patient)	1 (2.6%)	CR
	EMAEP	1 (2.6%)	CR
High-risk GTN (n=7)	EMACO	7 (100%)	6 CR, 1 LFU

DISCUSSION

Our study aimed to describe the clinical profile, risk distribution, treatment approaches, and outcomes of patients with GTD at our centre. Most patients were young and presented early with typical symptoms and high hCG levels. Low-risk cases responded well to methotrexate, whereas high-risk patients achieved good remission with multi-agent chemotherapy. Overall, timely diagnosis and protocol-based management led to favourable outcomes.

In our study, most patients were young adults, predominantly nulliparous, and presented early in pregnancy, typically within the first trimester of pregnancy. Osborne et al. also reported that the predominant age groups were 20–29 years (48.6% methotrexate; 41.3% dactinomycin) and 30–39 years (29%, 37.6%), with only 6.5–10.1% above 40 years, and despite inclusion up to 59 years, most were of reproductive age.[11] Similarly, Gulia et al. found that 98% of low-risk and 96% of high-risk patients were younger than 40 years.[12] El-Helw et al. showed hydatidiform mole in 86.2% (before 2000) and 83.8% (2000–2006), and choriocarcinoma in 13.8% and 16.2%.[13] Jagtap et al. reported 57.14% of cases at 20–25 years, 32.46% at 25–30 years, 3.9% below 20 years, and 6.5% above 30 years.[14] Therefore, the collective data across various studies support our finding that younger, predominantly nulliparous women form the major affected group.

In our study, most patients were symptomatic at presentation, with bleeding per vaginum being the predominant complaint, followed by hyperemesis and abdominal pain, while a notable proportion were asymptomatic and diagnosed incidentally on ultrasonography. Similarly, Jagtap et al. documented bleeding per vaginum as the most common symptom (94.8%), followed by amenorrhea (92.2%), pain (62.34%), hyperemesis (10.39%), passage of vesicles

(6.5%), and hyperthyroidism (2.6%), reflecting the classical symptom profile of GTD.[14] Mulik et al. reported amenorrhea in 100%, bleeding per vaginum in 68.2%, abdominal pain in 31.8%, and hyperemesis, passage of vesicles, and hyperthyroid features each in 9.1%.[15] Thus, the symptom profile observed in our study aligns well with classical patterns consistently reported in the literature.

In our study, most patients had markedly elevated pre-evacuation and pre-treatment hCG levels, with the majority falling in the higher range and only a small proportion showing low values. Similarly, Osborne et al. reported hCG levels from <10.1 to >100,000 mIU/mL, with most in the 10,000.1–100,000 range (32.7% methotrexate; 35.8% dactinomycin), followed by 1,500–5,000 and 100–1,500, while only 5.6% and 3.7% reached 100,000–1,000,000.[11] Gulia et al. showed 73% of high-risk patients had hCG >100,000 IU/L versus 32% in low-risk, with <1,000 and 1,000–10,000 levels uncommon in high-risk cases.[12] Jagtap et al. observed 53.25% with 50,000–100,000 mIU/mL, 44.15% with 100,000–500,000 mIU/mL, only 2.6% with 500,000–1,000,000 mIU/mL, and a mean of 267,837 mIU/mL.[14] Also, Mulik et al. documented 72.7% with >100,000 IU/L and 27.3% between 10,000–100,000 IU/L, with none below 10,000 IU/L.[15] Thus, the overall trends confirm that markedly elevated hCG levels are a consistent and defining characteristic in GTD patients across studies.

In our study, most patients were classified as having low-risk GTN, whereas a smaller proportion fell into the high-risk category. Similarly, Osborne et al. reported WHO scores ranging from 0 to 6, with most patients clustering in scores 0–3; scores 0 and 1 accounted for 50.5% (methotrexate) and 46.8% (dactinomycin), while higher scores (5–6) formed only approximately 7–8%.[11] In contrast, Alifrangis et al. included only high-risk patients (FIGO ≥6), most falling into scores 7–9 (65.7%) and 10–12 (19.3%), with invasive mole forming 57% and choriocarcinoma 43%; lung and brain metastases were frequent at 70% and 11.6%, respectively.[16]

Gulia et al. described 48 low-risk and 22 high-risk cases, with low-risk patients mainly at FIGO stage I (75%), while high-risk cases spanned stages II–IV, reflecting differing tumour burden and metastatic spread.[12] Moreover, El-Helw et al. reported similar patterns, with low-risk cases accounting for 91.6% before 2000 and 90% between 2000 and 2006, and FIGO staging showing a predominance of early disease.[13] Overall, the risk patterns reported in various studies align with our observations, reinforcing the typical distribution between low- and high-risk categories.

In our study, the treatment outcomes were favourable. Most low-risk patients responded well to methotrexate, with additional therapies achieving complete remission in those who required them. High-risk patients treated with EMACO also showed good overall response rates. Similarly, Schink et al. reported high complete response rates with actinomycin-D (78.6%) and methotrexate (88.5%), low failure (14.3%, 7.7%) and recurrence (9.1%, 8.7%) rates, with all patients alive and median cycles of 6 (IV Act-D), 7 (IM MTX), and 6 (IV MTX).[17] In contrast, Osborne et al. observed lower complete response rates of 53.3% (methotrexate) and 69.7% (dactinomycin), with higher non-response (44.9%, 26.6%) and improved outcomes in those with lower WHO scores and hCG levels.[11]

Alifrangis et al. showed strong high-risk outcomes with EMA/CO, including 86.4% primary cure, 94.3% overall survival, minimal early deaths (0.7%), no treatment-related mortality, and 20% relapse/resistance.[16] Gulia et al. demonstrated complete response rates of 97.2% (low-risk) and 72.7% (high-risk), with progressive disease only in high-risk (9%), and grade 3/4 neutropenia higher in EMA/CO cycles (31.5% low-risk; 13.6% high-risk).12 Furthermore, El-Helw et al. reported complete response rates of 77% and 79.5% (low- vs. high-risk) before 2000, and 61.6% and 75% between 2000 and 2006; second-line therapy achieved 92.8% and 87.9% complete response, mortality was low (3.2%, 1.2%), and survival remained high (96.6–98.8%).[13] Treatment response patterns remain uniformly encouraging across different cohorts, reflecting the robustness of current therapeutic approaches.

Limitations

This study was limited by its single-centre design, which may restrict the generalisability of the findings. Incomplete follow-up and reliance on available clinical records may have introduced reporting bias and prevented long-term outcome assessments.

CONCLUSION

Most patients presented in the 20–30-year age group with early gestational age and typical symptoms, such as vaginal bleeding. Risk-stratified management demonstrated high remission rates, especially among low-risk cases treated with methotrexate. High-risk patients also respond well to multi-agent chemotherapy. Timely diagnosis, appropriate protocol-based treatment, and regular β-hCG monitoring contributed to favourable outcomes in this cohort. Future studies with larger, multicentre cohorts and long-term follow-up could provide deeper insights into recurrence patterns and survival trends.

REFERENCES

1. Strickland AL, Gwin K. Gestational trophoblastic disease-rare, sometimes dramatic, and what we know so far. Semin Diagn Pathol 2022;39:228–37. https://doi.org/10.1053/j.semdp.2022.03.002.
2. Ratanakaew A, Wasinghon P. Prognostic scoring and outcome of gestational trophoblastic disease patients. J Clin Gynecol Obstet 2023;12:46–51. https://doi.org/10.14740/jcgo876.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556

3. Joyce CM, Fitzgerald B, McCarthy TV, Coulter J, O'Donoghue K. Advances in the diagnosis and early management of gestational trophoblastic disease. BMJ Med 2022;1:e000321. https://doi.org/10.1136/bmjmed-2022-000321.

4. Soper JT. Gestational trophoblastic disease: Current evaluation and management. Obstet Gynecol 2021;137:355–70. https://doi.org/10.1097/aog.0000000000004240.

5. Abebaw N, Biset G, Yimer N, Gezie H, Workneh M, Mulugeta C, et al. Magnitude and its associated factors of gestational trophoblastic disease in East African countries, systematic review and meta-analysis. Front Oncol 2025;15:1515246. https://doi.org/10.3389/fonc.2025.1515246.

6. Shaaban AM, Rezvani M, Haroun RR, Kennedy AM, Elsayes KM, Olpin JD, et al. Gestational trophoblastic disease: Clinical and imaging features. Radiographics 2017;37:681–700. https://doi.org/10.1148/rg.2017160140.

7. National Cancer Institute. Gestational Trophoblastic Disease Treatment (PDQ®)–Health Professional Version. Bethesda (MD): National Cancer Institute; updated 2025. Available from: https://www.cancer.gov/types/gestational-trophoblastic/hp/gtd-treatment-pdq

8. Ngan HYS, Seckl MJ, Berkowitz RS, Xiang Y, Golfier F, Sekharan PK, et al. Diagnosis and management of gestational trophoblastic disease: 2025 update. Int J Gynaecol Obstet 2025;171 Suppl 1:78–86. https://doi.org/10.1002/ijgo.70275.

9. Shahzadi M, Khan SR, Tariq M, Baloch SS, Shahid A, Moosajee M, et al. Review of current literature on gestational trophoblastic neoplasia. J Egypt Natl Canc Inst 2023;35:37. https://doi.org/10.1186/s43046-023-00195-y.

10. Bruce S, Sorosky J. Gestational trophoblastic disease. Treasure Island (FL): StatPearls Publishing; 2025. https://www.ncbi.nlm.nih.gov/books/NBK470267/

11. Osborne RJ, Filiaci V, Schink JC, Mannel RS, Alvarez Secord A, Kelley JL, et al. Phase III trial of weekly methotrexate or pulsed dactinomycin for low-risk gestational trophoblastic neoplasia: a gynecologic oncology group study. J Clin Oncol 2011;29:825–31. https://doi.org/10.1200/JCO.2010.30.4386.

12. Gulia S, Bajpai J, Gupta S, Maheshwari A, Deodhar K, Kerkar RA, et al. Outcome of gestational trophoblastic neoplasia: experience from a tertiary cancer centre in India. Clin Oncol (R Coll Radiol) 2014;26:39–44. https://doi.org/10.1016/j.clon.2013.08.010.

13. El-Helw LM, Coleman RE, Everard JE, Tidy JA, Horsman JM, Elkhenini HF, et al. Impact of the revised FIGO/WHO system on the management of patients with gestational trophoblastic neoplasia. Gynecol Oncol 2009;113:306–11. https://doi.org/10.1016/j.ygyno.2009.02.006.

14. Jagtap SV, Aher V, Gadhiya S, Jagtap SS. Gestational trophoblastic disease: clinicopathological study at a tertiary care hospital. J Clin Diagn Res 2017;11:EC27–EC30. https://pubmed.ncbi.nlm.nih.gov/28969138/

15. Mulik J, Choudhary A. Clinical study of gestational trophoblastic disease in a tertiary care hospital. Int J Reprod Contracept Obstet Gynecol 2020;9:2964. https://doi.org/10.18203/2320-1770.ijrcog20202741.

16. Alifrangis C, Agarwal R, Short D, Fisher RA, Sebire NJ, Harvey R, et al. EMA/CO for high-risk gestational trophoblastic neoplasia: good outcomes with induction low-dose etoposide-cisplatin and genetic analysis. J Clin Oncol 2013;31:280–6. https://doi.org/10.1200/JCO.2012.43.1817.

17. Schink JC, Filiaci V, Huang HQ, Tidy J, Winter M, Carter J, et al. An international randomized phase III trial of pulse actinomycin-D versus multi-day methotrexate for the treatment of low risk gestational trophoblastic neoplasia; NRG/GOG 275. Gynecol Oncol 2020;158:354–60. https://doi.org/10.1016/j.ygyno.2020.05.013.