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Study on the Clinical Presentation and Follow-Up of Gestational Trophoblastic Disease

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Abstract

Background: Gestational Trophoblastic Disease (GTD) encompasses a spectrum of pregnancy-related disorders, ranging from benign hydatidiform mole to malignant choriocarcinoma, and poses diagnostic and therapeutic challenges, particularly in resource-limited settings. The purpose of the study was to assess the clinical presentation and follow-up outcomes of patients diagnosed with Gestational Trophoblastic Disease (GTD). ***Aim of the study:*** The aim of the study was to evaluate the clinical presentation and follow-up outcomes of patients diagnosed with Gestational Trophoblastic Disease (GTD). ***Methods:*** This descriptive cross-sectional study, conducted at the Department of Obstetrics and Gynaecology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, from November 2012 to November 2013, included 70 GTD patients. Data were collected using a structured questionnaire, analyzed via SPSS, and ethical approval was obtained with assurances of confidentiality and voluntary participation. ***Results:*** Among 70 patients with GTD, 55.71% were aged 21–30 years, and 91.43% came from below-average income groups. The most common symptom in molar pregnancies was per vaginal bleeding (55.56%), while persistent mole and choriocarcinoma patients frequently presented with bleeding and lower abdominal pain (52%). A large proportion (77.78%) of molar pregnancies had uterine sizes larger than the period of gestation. Regular follow-up was observed in 74% of patients, and 100% underwent serum β-hCG testing. Most hydatidiform mole patients (80%) achieved remission, while 10% of choriocarcinoma cases resulted in death. ***Conclusion:*** Consistent monitoring and early detection significantly improve the clinical outcomes of patients diagnosed with Gestational Trophoblastic Disease (GTD).

Keywords: Gestational Trophoblastic Disease, Clinical Presentation, Follow-Up, Hydatidiform Mole, Choriocarcinoma.

INTRODUCTION

Gestational Trophoblastic Disease (GTD) encompasses a diverse group of pregnancy-related disorders characterized by the abnormal growth of trophoblastic tissue. It includes both benign and malignant forms, such as hydatidiform mole (complete and partial), invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT) [1-3]. Among these, the malignant forms—collectively termed Gestational Trophoblastic Neoplasia (GTN)—have the potential for distant metastases if untreated [4]. Marked by the proliferation of trophoblastic cells and persistent secretion of human chorionic gonadotropin (hCG) [5], GTN exhibits diverse biological behavior, with invasive mole and choriocarcinoma responding well to chemotherapy [6], while PSTT and ETT show relative resistance to treatment. These differences underscore the complexity of GTD and its varied clinical presentation.

GTN can arise after any pregnancy, although the highest risk follows a molar pregnancy, particularly a complete hydatidiform mole (CHM) [7]. It is estimated

that 50–80% of GTN cases originate from hydatidiform moles, with CHM having a higher likelihood of progressing to postmolar GTN [8]. The disease's presentation varies, often mimicking other conditions, as it affects multiple organs and systems [9]. In developed regions, ultrasonography and serial hCG measurements are routine diagnostic tools for early pregnancy complications, facilitating timely GTD detection [6, 10-12]. However, in resource-limited settings, the lack of access to these technologies necessitates greater clinical awareness and a high index of suspicion to ensure early diagnosis. Early detection not only improves prognosis but also guides effective treatment strategies, particularly the use of hCG as a biomarker to monitor disease progression.

The treatment of GTN has seen remarkable success, with cure rates exceeding 90% globally and even higher in specialized centers [13]. Low-risk GTN is typically managed with single-agent chemotherapy, such as methotrexate (MTX) or actinomycin D (ActD), tailored to the disease's risk classification [2]. Regular follow-up remains essential, as persistent disease is often identified through serial hCG measurements, with a plateau or rise signaling the need for further intervention [14]. Early chemotherapy administration at fixed intervals minimizes resistance and reduces the need for intensive multi-agent therapies. Vigilant follow-up is equally critical in detecting recurrences early, ensuring optimal outcomes and reinforcing the importance of sustained post-treatment care.

GTD represents a spectrum of rare yet treatable conditions, posing unique diagnostic and therapeutic challenges, particularly in resource-constrained regions. Despite significant advancements in diagnostic and therapeutic strategies, gaps persist in understanding the disease's presentation, progression, and outcomes across diverse populations. This study aims to assess the clinical presentation and follow-up outcomes of patients diagnosed with Gestational Trophoblastic Disease (GTD).

Objective

- The aim of the study was to evaluate the clinical presentation and follow-up outcomes of patients diagnosed with Gestational Trophoblastic Disease (GTD).

METHODOLOGY AND MATERIALS

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. It included all patients diagnosed with gestational trophoblastic disease (GTD) during the study period, with a sample size of 70 cases.

Inclusion Criteria:

- Fresh cases of GTD (hydatidiform mole, invasive mole, choriocarcinoma, and PSTT) presenting for the first time for treatment.
- Previously incompletely treated cases of GTD.
- Recurrent cases of GTD.

Exclusion Criteria:

- Patients with other known gynecological malignancies.
- Patients with severe chronic illnesses unrelated to GTD that could affect study outcomes.

Informed consent was obtained from all participants, ensuring voluntary participation and confidentiality. Data were collected using a structured, pretested questionnaire that was designed based on the research objectives. Patient history and clinical examinations were thoroughly conducted. Data collection took place over one year, with a total sample size of 70. The data were verified for consistency, entered into SPSS software, and analyzed for means, medians, standard deviations, and percentages. Findings were presented using tables, pie charts, and graphs in MS Excel. The study was approved by the ethical committee of Sir Salimullah Medical College & Mitford Hospital, and participants were assured of their right to decline participation and that their information would be used solely for research purposes.

RESULTS

Table 1: Incidence of GTD

Total Obstetric Admissions	No. of Patients with GTD	Incidence
10,320	70	6.7 per thousand hospital deliveries

During the study period, a total of 10,320 obstetric patients were admitted, and 70 patients were diagnosed with Gestational Trophoblastic Disease (GTD), resulting in an incidence of 6.7 per thousand hospital deliveries.

Table 2: Demographic Characteristics of Patients with GTD (n=70)

Variable			Percentage (%)
Age Distribution	<20 years	18	25.71%
	21–30 years	39	55.71%
	31–40 years	13	18.57%
	>40 years	1	1.43%
Parity Distribution	Primi	25	35.71%
	G2–G4	36	51.43%
	G5–G6	6	8.57%%
	G7–G8	3	4.29%
Socio-economic Status	Below Average Income Group	64	91.43%
	Average Income Group	6	8.57%
	Above Average Income Group	0	0.00%
Blood Group Distribution	A	34	48.57%
	B	17	24.29%
	O	14	20.00%
	AB	5	7.14%
Hemoglobin Levels (g/dL)	8–9.9	31	44.29%
	6.5–7.9	25	35.71%
	<6.5	10	14.29%
	>10	4	5.71%

The majority of the patients (55.71%) were aged between 21 and 30 years, followed by 25.71% under 20 years, 18.57% aged 31 to 40 years, and only 1.43% above 40 years. Regarding parity, 35.71% were primigravida, 51.43% had 2–4 previous pregnancies, 8.57% had 5–6 pregnancies, and 4.29% had 7–8 pregnancies. Socio-economic analysis showed that 91.43% of the patients came from below-average income groups, 8.57% were from average income groups, and none belonged to above-average income families. Blood group distribution revealed that 48.57% of the patients had blood group A, 24.29% had group B, 20.00% had group O, and 7.14% had group AB. Hemoglobin levels indicated that 44.29% of patients had levels between 8–9.9 g/dL, 35.71% had levels of 6.5–7.9 g/dL, 14.29% had levels below 6.5 g/dL, and only 5.71% had hemoglobin levels above 10 g/dL.

Table 3: 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	25	55.56%
	P/V bleeding with lower abdominal pain	3	6.67%
	P/V bleeding with passage of vesicles	10	22.22%
	Amenorrhoea with exaggerated pregnancy symptoms	6	13.33%
	Amenorrhoea with preeclampsia	1	2.22%
Persistent Mole and Choriocarcinoma	P/V bleeding with lower abdominal pain	13	52.00%
	Amenorrhoea with lower abdominal pain	7	28.00%
	Amenorrhoea with breathlessness	3	12.00%
	P/V bleeding with neurological feature	1	4.00%
	P/V bleeding with vaginal nodule	1	4.00%

Among patients with molar pregnancy (n=45), the most common presenting symptom was P/V bleeding, observed in 25 cases (55.56%), followed by P/V bleeding with passage of vesicles in 10 cases (22.22%) and P/V bleeding with lower abdominal pain in 3 cases (6.67%). Amenorrhea was reported in 7 patients (15.55%), with 6 cases (13.33%) associated with exaggerated pregnancy symptoms and 1 case (2.22%) with preeclampsia. Among patients with persistent mole and choriocarcinoma (n=25), P/V bleeding with lower abdominal pain was the most frequent symptom, reported in 13 cases (52%). Amenorrhea with lower abdominal pain occurred in 7 cases (28%), while amenorrhea with breathlessness was noted in 3 cases (12%). P/V bleeding with neurological features and vaginal nodules was present in 2 cases (8%), each accounting for 4%.

Table 4: Correlation between Uterine Size and Gestational Period in Molar Pregnancy (n = 45)

Height of Uterus	No. of Cases (n)	Percentage (%)
Uterus more than period of gestation	35	77.78%
Uterus corresponds with period of gestation	9	20.00%
Uterus less than period of gestation	1	2.22%

Out of 45 cases of molar pregnancies, in 35 patients (77.78%) the uterus was larger than the period of gestation. In 9 patients (20.00%), the uterus corresponded with the period of gestation, and in 1 patient (2.22%) it was smaller than the period of gestation.

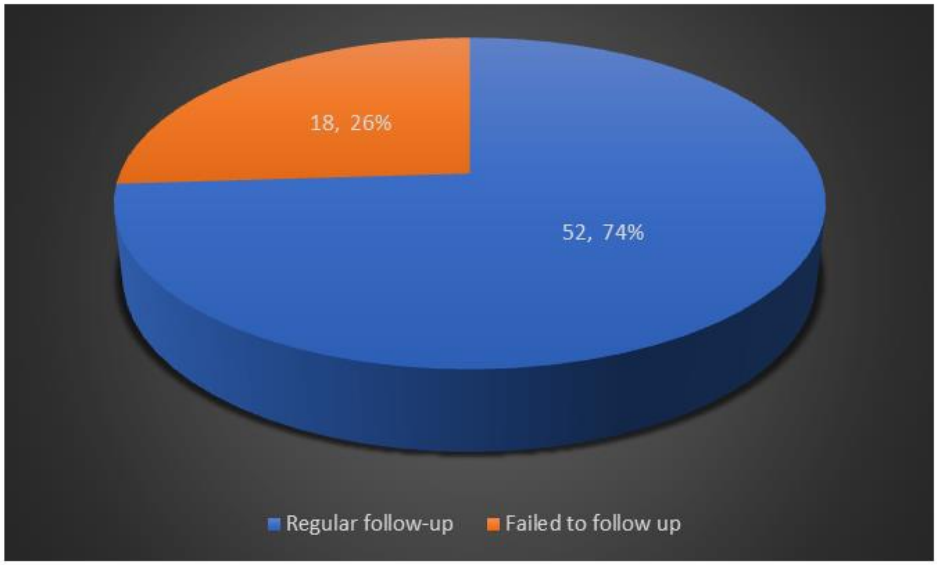

Figure 1: Follow-up of Patients with GTD (n=70)

All patients with GTD were advised to attend regular follow-up. Among them, 52 patients (74%) adhered to regular follow-up, while 18 patients (26%) failed to follow up.

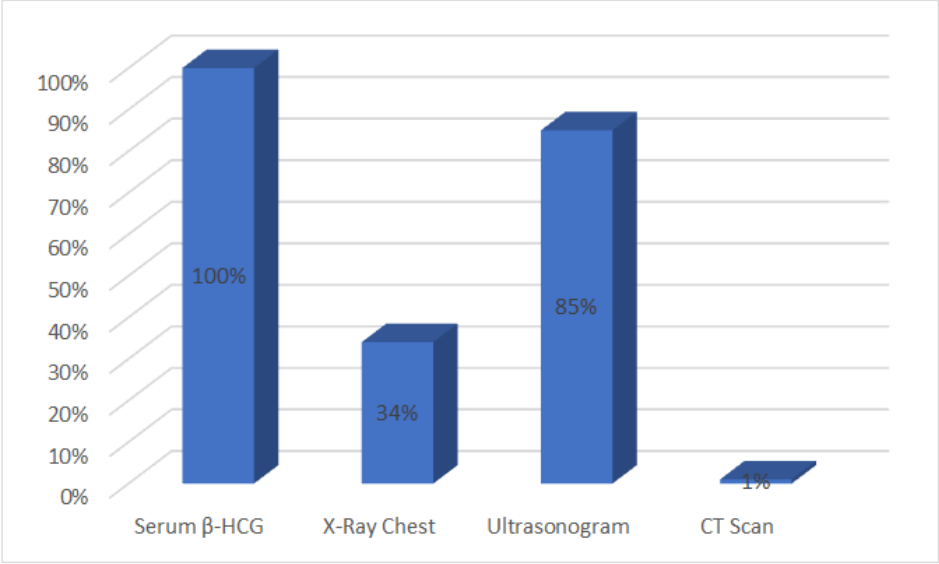

Figure 2: Laboratory Investigations Used for Follow-up in GTD (n=70)

Among the patients who underwent laboratory investigations (n=70), all (100%) had a serum β-hCG test performed. Additionally, 24 patients (34%) underwent an X-ray of the chest, while 60 patients (85%) had an ultrasonogram of the uterus and adnexae. A CT scan was conducted for 1 patient (1%) who presented with unconsciousness.

Table 5: Fates of GTD During Follow-Up

Type of GTD	Total Patients	No. of Patients Appeared for Follow-Up	Failed to Follow-Up	Remission	Persistent Mole	Choriocarcinoma	Death
H. Mole	45	31	14	25	4	1	0
Persistent Mole	14	11	3	11	0	0	0
Choriocarcinoma	11	10	1	9	0	0	1

Out of the total 45 patients diagnosed with hydatidiform mole (H. Mole), 31 patients (69%) appeared for follow-up, while 14 patients (31%) failed to do so. Among those who followed up, 25 patients (80%) went into remission, 4 (13%) had persistent mole, and 1 patient (3%) developed choriocarcinoma. There were no deaths in this group. For persistent mole, 14 patients were diagnosed, with 11 (79%) appearing for follow-up and 3 (21%) failing to follow up. All 11 patients who followed up had remission, and there were no cases of persistent mole or choriocarcinoma. Among the 11 choriocarcinoma patients, 10 (91%) came for follow-up, with 1 (9%) failing to follow up. Of those who followed up, 9 (90%) achieved remission, and 1 patient (10%) died.

DISCUSSION

Gestational Trophoblastic Disease (GTD) presents a significant clinical challenge in Bangladesh, characterized by a range of disorders including hydatidiform mole, invasive mole, and choriocarcinoma. The incidence of GTD remains high, underscoring the need for early detection and effective management strategies. This study aimed to evaluate the clinical presentation and follow-up outcomes of 70 patients diagnosed with GTD at Sir Salimullah Medical College and Mitford Hospital, Dhaka, over a one-year period. The findings revealed a predominance of molar pregnancies, with a notable percentage of patients presenting with symptoms such as vaginal bleeding and abdominal pain. The study also emphasized the importance of regular follow-up, with a majority of patients adhering to recommended visits, leading to favorable outcomes in terms of remission. However, challenges in follow-up adherence and varied clinical presentations underline the need for improved patient education and management protocols to ensure better long-term outcomes.

In this study, the majority of patients (55.71%) were aged 21-30 years, with a notable proportion (25.71%) under 20 years and fewer patients aged 31-40 years (18.57%). Regarding parity, 35.71% were primigravida, and 51.43% had 2-4 previous pregnancies. Socio-economically, 91.43% of patients were from below-average income groups, and blood group distribution showed a predominance of group A (48.57%), followed by group B (24.29%), O (20%), and AB (7.14%). Hemoglobin levels were low in most patients, with 44.29% having levels between 8-9.9 g/dL and 35.71% between 6.5-7.9 g/dL. These findings align with those of Neelakanthi *et al.,* [15] in their study, where the mean age was 21.56 ± 2.9 years, and most patients were from low-income backgrounds. Both studies emphasize the significance of age, socio-economic status, and the need for regular follow-up in managing GTD effectively across different settings.

In our study, among patients with molar pregnancy (n=45), the most common presenting symptom was P/V bleeding (55.56%), followed by P/V bleeding with the passage of vesicles (22.22%) and P/V bleeding with lower abdominal pain (6.67%). Amenorrhea was reported in 15.55% of cases, with exaggerated pregnancy symptoms in 13.33% and preeclampsia in 2.22%. These findings are consistent with the study by Mdoe *et al.,* [16], which also highlighted significant occurrences of these clinical presentations in women with GTD. 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 this study, out of 45 cases of molar pregnancies, 35 patients (77.78%) had a uterus larger than the period of gestation, 9 patients (20.00%) had a uterus corresponding with the period of gestation, and 1 patient (2.22%) had a uterus smaller than the period of gestation. Similarly, in a study by Elias *et al.,* [17], it was found that the majority of patients with complete hydatidiform mole (CHM) presented with a uterus size larger than expected for the gestational period. This similarity underscores the common clinical feature of uterine enlargement in molar pregnancies, which is crucial for early diagnosis and management. The consistent observation in both studies highlights the importance of considering uterine size as a key diagnostic indicator for molar pregnancies and other forms of gestational trophoblastic disease. Study by Soto-Wright *et al.,* [18] did not support this evidence where excessive uterine size was present in 28% and 15% patients respectively. The marked difference of study with international studies is due to late diagnosis of the disease, which is due to lack of awareness and

education of the patient, inappropriate investigation facilities.

In our study, all patients with GTD were advised to attend regular follow-up, with adherence observed in 52 patients (74%) while 18 patients (26%) failed to follow up. Among the 45 patients diagnosed with hydatidiform mole, 31 (69%) attended follow-up, of whom 25 (80%) achieved remission, 4 (13%) developed persistent mole, and 1 (3%) progressed to choriocarcinoma, with no reported deaths. Similarly, out of 14 patients with persistent mole, 11 (79%) attended follow-up, all of whom achieved remission, with no further cases of persistent mole or choriocarcinoma. For the 11 choriocarcinoma cases, 10 (91%) adhered to follow-up, 9 (90%) achieved remission, and 1 (10%) patient succumbed during chemotherapy due to brain metastases. Findings from Mungan *et al.*, [19], where 100% follow-up adherence was achieved with an 85.5% remission rate, further emphasize the impact of consistent surveillance on outcomes. These patterns highlight the critical role of structured follow-up in achieving favorable outcomes in GTD management.

This study underscores the importance of early diagnosis, effective management, and regular follow-up for patients with Gestational Trophoblastic Disease (GTD) in Bangladesh. While the majority adhered to follow-up, non-compliance remains a challenge. The findings emphasize the critical role of follow-up in achieving favorable outcomes, with remission rates improving significantly among patients who attended. Enhanced patient education and awareness are essential to improve follow-up adherence and ensure better long-term outcomes for GTD patients in Bangladesh.

Limitations of the study

This study had several limitations:

- A substantial number of patients missed follow-ups, likely due to socio-economic constraints, low educational levels, and limited health awareness.
- Key investigations, such as B-hCG testing, were inconsistently performed because free testing facilities were unavailable in government hospitals.
- The lack of a standardized molar card system affected the accuracy of patient record-keeping.
- The small sample size limits the ability to generalize findings, and a larger cohort would offer more comprehensive insights into specific subgroups.

CONCLUSION

This study evaluated the clinical presentation and follow-up outcomes of 70 patients diagnosed with Gestational Trophoblastic Disease (GTD). The incidence of GTD was found to be 6.7 per thousand hospital deliveries. The majority of patients were aged between 21 and 30 years and predominantly came from below-average income groups. The most common presenting symptom for molar pregnancies was P/V bleeding, while persistent mole and choriocarcinoma patients frequently experienced P/V bleeding and lower abdominal pain. A significant proportion of molar pregnancies exhibited uterine enlargement beyond the gestational period. Regular follow-up was crucial, with 74% of patients adhering to it, ensuring a majority underwent necessary investigations like serum β-HCG tests and ultrasonograms. Outcomes indicated high remission rates for hydatidiform mole, persistent mole, and choriocarcinoma with appropriate follow-up, emphasizing the importance of consistent monitoring and early detection in managing GTD effectively.

REFERENCES

1. Lurain, J. R. (2010). Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *American journal of obstetrics and gynecology*, *203*(6), 531-539.
2. Seckl, M. J., Sebire, N. J., Fisher, R. A., Golfier, F., Massuger, L., Sessa, C., & ESMO Guidelines Working Group. (2013). Gestational trophoblastic disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology*, *24*, vi39-vi50.
3. Ngan, H. Y., Seckl, M. J., Berkowitz, R. S., Xiang, Y., Golfier, F., Sekharan, P. K., & Lurain, J. R. (2015). Update on the diagnosis and management of gestational trophoblastic disease. *International Journal of Gynecology & Obstetrics*, *131*, S123-S126.
4. Froeling, F. E., & Seckl, M. J. (2014). Gestational trophoblastic tumours: an update for 2014. *Current oncology reports*, *16*, 1-10.
5. Seckl, M. J., Sebire, N. J., & Berkowitz, R. S. (2010). Gestational trophoblastic disease. *The Lancet*, *376*(9742), 717-729.
6. Adeleye, J. A., & Osinusi, B. O. (1980). Epidemiological features of malignant trophoblastic diseases in Ibadan Nigeria. *Singapore J Obstet Gynaecol*, 11, 55-58.
7. Elias, K. M., Berkowitz, R. S., & Horowitz, N. S. (2019). State-of-the-art workup and initial management of newly diagnosed molar pregnancy and postmolar gestational trophoblastic neoplasia. *Journal of the National Comprehensive Cancer Network*, *17*(11), 1396-1401.
8. Ramírez, L. A. C., Maestá, I., Bianconi, M. I., Jankilevich, G., Otero, S., Mejía, C. R. V., ... & Berkowitz, R. S. (2022). Clinical Presentation, Treatment Outcomes, and Resistance-related Factors in South American Women with Low-risk Postmolar Gestational Trophoblastic Neoplasia. *Revista Brasileira de Ginecologia e Obstetrícia*, *44*(08), 746-754.

9. Ekanem, E. I., Etuk, S. J., Itam, I. H., & Ekott, M. I. (2006). The clinical presentation of gestational trophoblastic disease in Calabar, Nigeria. *Global Journal of Medical Sciences*, *5*(1), 45-49.
10. Robert, F, John, A. B., & Sharma, A. (2000). Early pregnancy assessment, suspected trophoblastic disease. *Obstet Gynaecol*, *2*(2), 11-12.
11. Varma, T. R. (1990). Gestational Trophoblastic Disease. In: Varma, T. R., editor. Clinical Gynaecology. Edvard Arnold; p. 582-615.
12. Ma, H. K., & Wong, L. C. (1990). The modern management of reproductive diseases. *Recent Adv Obstet Gynaecol*, 3, 158.
13. Freitas, F., Braga, A., Viggiano, M., Velarde, L. G. C., Maesta, I., Uberti, E., ... & Berkowitz, R. S. (2020). Gestational trophoblastic neoplasia lethality among Brazilian women: a retrospective national cohort study. *Gynecologic Oncology*, *158*(2), 452-459.
14. Wolfberg, A. J., Berkowitz, R. S., Goldstein, D. P., Feltmate, C., & Lieberman, E. (2006). Postevacuation hCG levels and risk of gestational trophoblastic neoplasia in women with complete molar pregnancy. *Obstetrics & Gynecology*, *107*(3), 743.
15. Neelakanthi, A., & Lokeshchandra, H. C. (2020). Gestational Trophoblastic Disease: A Hospital-Based Prospective Study to Characterize Incidence, Risk Factors, Management and Review of Literature. *Indian Journal of Gynecologic Oncology*, *18*, 1-8.
16. Mdoe, M. B., Mwakigonja, A. R., & Mwampagatwa, I. (2023). Gestational trophoblastic disease and associated factors among women experiencing first trimester pregnancy loss at a regional referral hospital in central Tanzania: a cross-sectional study. *International Health*, *15*(3), 250-257.
17. Elias, K. M., Horowitz, N. S., & Berkowitz, R. S. (2023). First-Trimester Ultrasound in Gestational Trophoblastic Disease. In First-Trimester Ultrasound: A Comprehensive Guide 2023 Apr 14 (pp. 445-456). Cham: Springer International Publishing.
18. Soto-Wright, V., Bernstein, M., Goldstein, D. P., & Berkowitz, R. S. (1995). The changing clinical presentation of complete molar pregnancy. *Obstetrics & Gynecology*, *86*(5), 775-779.
19. Mungan, T., Kuşçu, E., Dabakoğlu, T., Şenöz, S., Uğur, M., & Çobanoglu, Ö. (1996). Hydatidiform mole: clinical analysis of 310 patients. *International Journal of Gynecology & Obstetrics*, *52*(3), 233-236.