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Epidemiological, Clinical, and Therapeutic Characteristics of Gestational Trophoblastic Disease in Eastern Madagascar: A Retrospective Study at a Tertiary Referral Center

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Abstract

Background: Gestational trophoblastic disease (GTD) comprises a spectrum of pregnancy-related disorders with marked geographical variation in incidence, being more frequent in low- and middle-income countries. Data from eastern Madagascar remain limited. **Objective:** To describe the epidemiological, clinical, paraclinical, and therapeutic characteristics of GTD managed at a tertiary referral hospital in eastern Madagascar. **Methods:** A retrospective descriptive study was conducted over a six-year period (January 2019 to December 2024) at the University Hospital Center of Analankininina Toamasina (CHUAT). All patients diagnosed with GTD based on histopathological findings and/or biological follow-up were included. Data were collected from medical records and analyzed using descriptive statistics. **Results:** A total of 53 cases of GTD were identified, including 42 hydatidiform moles and 11 cases of gestational trophoblastic neoplasia (GTN). The mean age was 29 ± 8.5 years, with a predominance of women aged 20 - 29 years. Vaginal bleeding was the most common presenting symptom (31/53). Initial serum human chorionic gonadotropin (hCG) levels exceeded 100,000 IU/L in 27 cases. According to FIGO scoring, 6 cases were classified as low risk and 5 as high risk. Uterine evacuation by curettage was performed in 41 patients. Chemotherapy was administered in all GTN cases. Complete remission was achieved in 41 patients, while 3 deaths were recorded. Subsequent pregnancy occurred in 13 patients.

Conclusion: GTD remains a significant health concern in eastern Madagascar, often diagnosed at advanced stages. Despite resource limitations, favorable outcomes can be achieved with appropriate management. Strengthening early diagnosis, pathology services, and follow-up systems is essential to improving prognosis.

Keywords

Gestational Trophoblastic Disease, Hydatidiform Mole, Gestational Trophoblastic Neoplasia, FIGO Score, Madagascar

1. Introduction

Gestational trophoblastic disease (GTD) encompasses a heterogeneous group of disorders arising from abnormal proliferation of placental trophoblastic tissue. It includes benign entities such as complete and partial hydatidiform mole, as well as malignant forms collectively referred to as gestational trophoblastic neoplasia (GTN), including invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor.

The global incidence of GTD varies widely, with higher rates reported in Asia, Africa, and Latin America compared with Europe and North America. However, epidemiological data remain scarce in many low-resource settings, including Madagascar, particularly outside the capital region.

Although GTN is highly sensitive to chemotherapy and associated with excellent cure rates, delayed diagnosis, limited access to diagnostic tools, and challenges in follow-up contribute to increased morbidity and mortality in low-resource settings.

This study aimed to describe the epidemiological, clinical, paraclinical, and therapeutic characteristics of GTD managed at a tertiary referral hospital in eastern Madagascar over a six-year period.

2. Methods

2.1. Study Design and Setting

A retrospective descriptive study was conducted at the Department of Gynecology and Oncology of the University Hospital Center of Analankininina Toamasina (CHUAT), a tertiary referral hospital in eastern Madagascar.

2.2. Study Period

January 2019 to December 2024.

2.3. Study Population

All patients diagnosed with GTD and managed at CHUAT during the study period were included.

2.4. Inclusion Criteria

Patients were included if they met at least one of the following criteria:

- Histopathological confirmation of hydatidiform mole or GTN.
- Availability of complete medical records: A "complete medical record" was defined as a file containing at least: demographic data, clinical presentation, serum hCG measurements, treatment information, and documented outcomes.

In cases without histopathological confirmation, hydatidiform mole was diagnosed based on typical clinical presentation (vaginal bleeding after amenorrhea), markedly elevated serum hCG levels, and characteristic ultrasound findings such as a "snowstorm" appearance.

The diagnosis of GTN was based on FIGO criteria, including one or more of the following:

- Plateau of serum hCG levels over at least three consecutive weeks.
- Rise in serum hCG levels over two consecutive weeks.
- Persistence of detectable hCG beyond 6 months after molar evacuation.
- Histological diagnosis of choriocarcinoma.

2.5. Data Collection

Data were extracted from medical records and included sociodemographic characteristics, obstetric history, clinical presentation, serum hCG levels, histopathological findings, FIGO score, treatment modalities, and outcomes.

Low-risk GTN patients (FIGO score ≤ 6) were treated with single-agent chemotherapy, primarily methotrexate-based regimens.

High-risk patients (FIGO score > 6) received combination chemotherapy, most commonly EMA-CO protocol when feasible.

Criteria for switching from single-agent to combination therapy included:

- Plateau or rise in hCG levels.
- Clinical or radiological evidence of disease progression.

After uterine evacuation, patients were monitored with weekly serum hCG measurements until normalization, followed by monthly monitoring for at least 6 months.

Complete remission was defined as normalization of serum hCG levels maintained for at least three consecutive weeks. Recurrence was defined as a subsequent rise in hCG after normalization. Subsequent pregnancies were identified through follow-up records and patient reports.

2.6. Statistical Analysis

Data were analyzed using descriptive statistics. Quantitative variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages.

2.7. Ethical Considerations

Confidentiality was maintained, and institutional authorization was obtained.

3. Results

A total of 16,755 medical records were screened across two departments of CHUAT. Among these, 5 were excluded due to incomplete data, including missing key variables such as serum hCG levels, treatment details, or outcome information. Finally, 53 cases of gestational trophoblastic disease met the inclusion criteria and were retained for analysis. These included 42 cases of hydatidiform mole (79.2%), primarily managed in the gynecology-obstetrics department, and 11 cases of gestational trophoblastic neoplasia managed in the oncology department.

Table 1. Sociodemographic and obstetric characteristics (n = 53).

Variable	Category	n	%
Age (years)	<20	7	13.2
	20 - 29	24	45.3
	30 - 39	16	30.2
	≥40	6	11.3
Occupation	Farmer	17	32.1
	Housewife	13	24.5
	Shopkeeper	13	24.5
	Student	5	9.4
	Others	5	9.4
Gravidity	Primigravida	9	17.0
	Paucigravida (2 - 4)	35	66.0
	Multigravida (5 - 6)	5	9.4
	Grand multigravida (≥7)	4	7.5
Parity	Nulliparous	13	24.5
	Primiparous	11	20.8
	Pauciparous (2 - 4)	24	45.3
	Multiparous (5 - 6)	3	5.7
	Grand multiparous (≥7)	2	3.8
History of abortion	Yes	20	37.7
	No	33	62.3
Index pregnancy	Molar pregnancy	50	94.3
	Normal pregnancy	1	1.9
	Miscarriage	2	3.8
Contraception	None	21	39.6
	Oral	8	15.1
	Injectable	20	37.7
	Implant	4	7.5

Table 1 summarizes sociodemographic and obstetric characteristics. Most patients were aged 20 - 29 years (45.3%). The majority were paucigravida (66.0%) and pauciparous (45.3%). A history of abortion was reported in 37.7% of cases. The index pregnancy was a molar pregnancy in 94.3% of cases. Contraceptive use was absent in 39.6% of patients.

Table 2 (Table 2(A) and Table 2(B)) presents clinical and paraclinical findings. Vaginal bleeding following amenorrhea was the most common presentation (58.5%). Serum hCG levels ≥100,000 IU/L were observed in 50.9% of patients. Notably, histopathological examination was unavailable in 77.4% of cases. Among the 11 patients with GTN, 2 presented with metastatic disease, with involvement of the lung in one case and the bladder in another.

Table 2. (A) Clinical presentation; (B) Paraclinical and prognostic features.

(A)			
Variable	**Category**	**n**	**%**
Clinical presentation	Bleeding after amenorrhea	31	58.5
	Persistent bleeding after molar evacuation	8	15.1
	Vomiting	6	11.3
	Vaginal expulsion of molar vesicles	3	5.7
	Elevated hCG	3	5.7
	Hemoptysis	1	1.9
	Hematuria	1	1.9
(B)			
Variable	**Category**	**n**	**%**
hCG level (IU/L)	<10,000	9	17.0
	10,000 - 100,000	17	32.1
	≥100,000	27	50.9
Histopathology	Hydatidiform mole	6	11.3
	Invasive mole	2	3.8
	Choriocarcinoma	4	7.5
	Not available	41	77.4
FIGO score	≤6	6	54.5
	>6	5	45.5

hCG = human chorionic gonadotropin.

Given the clinical and therapeutic differences between hydatidiform mole and gestational trophoblastic neoplasia, treatment modalities and outcomes were analyzed separately. The results are presented in Table 3(A) and Table 3(B).

Table 3. Treatment and outcomes according to disease type. (A) Hydatidiform mole (n = 42); (B) Gestational trophoblastic neoplasia (n = 11).

(A)			
Variable	**Category**	**n**	**%**
Initial management	Manual evacuation	5	11.9
	Uterine curettage	35	83.3
	Vacuum aspiration	2	4.8
	Hysterectomy	0	0
Outcomes	Remission	35	83.3
	Subsequent pregnancy	10	23.8
	Death	1	2.4
	Lost to follow-up	6	14.3
(B)			
Variable	**Category**	**n**	**%**
Initial management	Uterine curettage	6	54.5
	Hysterectomy	2	18.2
	No surgical management	3	27.3
Chemotherapy	Single-agent	6	54.5
	Combination	5	45.5
Outcomes	Remission	6	54.5
	Subsequent pregnancy	3	27.3
	Death	2	18.2
	Lost to follow-up	3	27.3

4. Discussion

This study provides one of the few detailed descriptions of gestational trophoblastic disease (GTD) in eastern Madagascar, highlighting important epidemiological, clinical, and therapeutic characteristics in a low-resource setting.

4.1. Sociodemographic Profile

The mean age and predominance of women aged 20 - 29 years are consistent with findings from other low- and middle-income countries, reflecting peak reproductive age [1] [2]. Although extreme maternal ages (<20 and ≥40 years) are recognized risk factors, their lower representation in this cohort may reflect demographic patterns and fertility distribution in the study population [3] [4].

The predominance of patients with low socioeconomic status, particularly farmers and housewives, reflects structural inequalities in access to healthcare. Similar observations have been reported in sub-Saharan Africa, where delayed diagnosis is often linked to limited access to reproductive health services and reduced health literacy [5] [6]. These determinants may contribute to late presentation and more advanced disease at diagnosis.

4.2. Obstetric History

The majority of patients were paucigravida (66.0%) and pauciparous (45.3%). While some studies report increased GTD risk in multiparous women, the relationship between parity and GTD remains inconsistent across populations [6]. A history of abortion was reported in 37.7% of cases, comparable to findings from other African series, although causal links between prior pregnancy loss and GTD are not firmly established [7] [8]. Notably, the index pregnancy was overwhelmingly a molar pregnancy (94.3%), consistent with the known epidemiology of GTD, where hydatidiform mole constitutes the most frequent entity [1].

Contraceptive use was suboptimal, with 39.6% of patients reporting no method, while injectable contraception was the most frequently used (37.7%). This pattern mirrors national trends in Madagascar and other sub-Saharan African countries, where access to modern contraceptive methods remains limited [9]. Although contraceptive methods are not directly associated with GTD risk, limited access to family planning and reproductive health services may contribute to delayed diagnosis and suboptimal monitoring of early pregnancies.

4.3. Clinical Presentation, Paraclinical Findings, and Prognostic Features

Clinically, vaginal bleeding following amenorrhea was the most common presenting symptom, consistent with classical descriptions of GTD [1] [2]. Persistent vaginal bleeding after molar evacuation was reported in 15.1% of cases, highlighting the need for close post-evacuation surveillance. Less frequent symptoms included vomiting (11.3%), vaginal expulsion of molar vesicles (5.7%), and persistent or rising serum hCG levels (5.7%). Rare presentations, such as hemoptysis and hematuria (each 1.9%), may indicate metastatic disease and underscore the potential severity of GTN in advanced stages [1] [10].

However, the high proportion of patients with serum hCG levels ≥ 100,000 IU/L suggests a substantial tumor burden at diagnosis, likely reflecting delayed presentation [4] [6]. Serum hCG measurement remains the cornerstone for both diagnosis and follow-up, particularly in settings where histopathological confirmation is limited [1] [11].

A major limitation of this study is the absence of histopathological confirmation in 77.4% of cases. This finding highlights significant constraints in pathology infrastructure in low-resource settings. Although diagnosis based on clinical presentation and hCG dynamics is acceptable in certain contexts, the lack of histopathology may lead to misclassification, inadequate risk stratification, and potential deviations from optimal management [1] [4] [12]. Similar challenges have been reported in other developing countries, emphasizing the urgent need to strengthen pathology services and standardize diagnostic pathways [5] [6].

4.4. Therapeutic Management and Clinical Outcomes

Regarding therapeutic management, uterine curettage was the mainstay of treat-

ment and remains the standard initial intervention for molar pregnancy worldwide [1]. This procedure allows rapid evacuation of trophoblastic tissue and facilitates subsequent monitoring. However, it carries risks such as hemorrhage, uterine perforation, and infection, particularly in settings lacking ultrasound guidance [12]. Despite these risks, curettage remains widely used in low-resource settings due to its accessibility, cost-effectiveness, and feasibility compared with more advanced techniques, such as minimally invasive suction evacuation or hysteroscopic techniques, which may not be available [4] [6].

Chemotherapy was administered in all patients with gestational trophoblastic neoplasia (GTN), in accordance with FIGO risk-adapted protocols [1]. The high remission rate observed in this study is consistent with the well-established chemosensitivity of GTN, even in metastatic stages [1]. These findings demonstrate that adherence to standardized treatment protocols can yield favorable outcomes, even in resource-constrained environments.

However, loss to follow-up remains a significant concern, affecting 17.0% of patients. This issue is commonly reported in low-resource settings and may compromise long-term outcomes, including detection of relapse and monitoring of subsequent pregnancies [6]. Strengthening follow-up systems and patient education is therefore essential.

Recent evidence has also highlighted the importance of long-term surveillance, as patients with a history of GTD may have an increased risk of subsequent malignancies, although this risk remains low [13]. Additionally, advances in imaging and diagnostic strategies have improved disease characterization and management in high-resource settings, but these innovations remain largely inaccessible in many low-income countries [11] [12].

Overall, this study underscores the dual reality of GTD management in low-resource settings: while effective treatments exist and outcomes can be favorable, major challenges persist in early diagnosis, access to histopathology, and continuity of care. Addressing these gaps is essential to further improve patient outcomes in Madagascar and similar contexts.

4.5. Strengths and Limitations

This study provides valuable data from an underrepresented region and contributes to the limited literature on GTD in Madagascar. However, this study has several limitations. Its retrospective design and single-center setting may introduce selection bias, particularly as a tertiary referral center likely receives more severe cases. Additionally, exclusion of incomplete records may have introduced selection bias. The high proportion of missing histopathological data limits diagnostic accuracy. Finally, loss to follow-up may affect the reliability of outcome assessment.

4.6. Implications for Practice

The study underscores the importance of early diagnosis through improved repro-

ductive health education and access to ultrasound and hCG monitoring. Strengthening regional reference centers and implementing standardized follow-up protocols could further improve outcomes. Additionally, enhancing access to family planning services may reduce the frequency of unmonitored pregnancies and facilitate early detection of abnormal gestations.

5. Conclusion

In eastern Madagascar, GTD predominantly affects women of reproductive age with limited parity and low socioeconomic status. Hydatidiform mole is the most common presentation, often diagnosed late. Despite resource limitations, adherence to standard surgical and chemotherapeutic protocols yields favorable outcomes. Strengthening early detection, patient follow-up, and reproductive health services is essential to further improve prognosis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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