

Hidden Moles in Early Pregnancy Loss: The Critical Role of Histopathology in First-Trimester Abortion Specimens

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ABSTRACT

Background: Early pregnancy loss (EPL) is commonly encountered in obstetric practice, yet routine histopathological examination (HPE) of products of conception (POC) is often neglected. Occult molar pregnancies may clinically mimic spontaneous abortions and remain undiagnosed without HPE, predisposing women to the risk of gestational trophoblastic neoplasia (GTN).

Objective: This study aims to describe the spectrum of gestational trophoblastic disease (GTD) in a tertiary-care centre and assess the prevalence of clinically unsuspected molar pregnancies among first-trimester abortion specimens.

Methods: A cross-sectional study was conducted from October 2024 to November 2025 at a tertiary teaching hospital in Western India. Two cohorts were included: One with 55 histologically confirmed GTD cases, and second with 255 consecutively submitted first-trimester abortion specimens. Clinical presentation, ultrasound findings, β -hCG levels, and histopathological features were analysed.

Results: Among 55 GTD cases, partial hydatidiform mole (PHM) accounted for 52.72%, complete hydatidiform mole (CHM) 43.63%, and invasive mole (IM) 3.63%. Post-molar GTN occurred in 7.27%. In the EPL cohort, none were clinically or ultrasonographically suspected to have molar pregnancy; however, HPE detected molar pathology in 5 cases (1.96%), including 2 CHM and 3 PHM-equivalent to one occult mole per 51 abortion specimens. A clinically significant proportion of molar pregnancies present as EPL and remain undiagnosed without HPE.

Conclusion: Routine histopathological evaluation of all first-trimester abortion specimens is essential to ensure timely diagnosis and prevent progression to GTN.

Key words: Abortion, pregnancy loss, molar pregnancy, Histopathology

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INTRODUCTION

Early pregnancy loss (EPL), defined as pregnancy loss before 12 completed weeks of gestation, accounts for up to 20% of all clinically recognized pregnancies [1]. Although EPL is frequently managed with medical or surgical evacuation, routine histopathological examination (HPE) of products of conception (POC) is not universally practiced, particularly in low-resource settings [2,3]. The assumption that most EPLs are due to chromosomal abnormalities has contributed to this oversight.

Gestational trophoblastic disease (GTD) encompasses a spectrum ranging from complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM) to invasive mole (IM), choriocarcinoma, and placental site trophoblastic tumour [4]. Molar pregnancies are clinically significant because they may progress to gestational trophoblastic neoplasia (GTN), which can be locally invasive or metastatic but is highly treatable when detected early [5]. The clinical presentation of molar pregnancy, including vaginal bleeding, abdominal pain, or hyperemesis is nonspecific and similar to EPL [6]. Ultrasonography (USG) can detect characteristic findings in CHM but is less sensitive in early gestation and in PHM, where features often overlap with missed or incomplete abortions. Thus, histopathology remains the gold standard for diagnosis.

Failure to diagnose molar pregnancy results in inadequate β -hCG surveillance and increases the risk of delayed GTN detection [7]. Approximately 3% of POC specimens from first-trimester abortions contain occult molar tissue [8]. This study evaluates the spectrum of GTD at a tertiary-care hospital in Western India and quantifies the burden of occult molar pregnancies among first-trimester abortion specimens, highlighting the critical role of routine HPE.

METHODOLOGY

Study Design and Setting

This cross-sectional observational study was conducted in the Departments of Obstetrics and Gynecology and Pathology of a tertiary-care teaching hospital in Western India over a period extending from October 2024 to November 2025. The study aimed to evaluate the diagnostic concordance between clinical, ultrasonographic, and histopathological findings in patients presenting with early pregnancy loss and gestational trophoblastic disease.

Study Cohorts

A total of 310 patients were included in the study and categorized into two cohorts. The GTD cohort comprised 55 patients diagnosed based on clinical features,

ultrasonographic findings, elevated serum β -human chorionic gonadotropin (β -hCG) levels, and subsequent histopathological confirmation. The EPL cohort consisted of 255 women presenting with first-trimester pregnancy loss, including missed abortion, incomplete abortion, or anembryonic gestation, whose products of conception POC were submitted for routine histopathological examination.

Inclusion Criteria

Women presenting with first-trimester pregnancy loss at or before 12 weeks of gestation were included in the study. In addition, all cases with histopathologically confirmed gestational trophoblastic disease were enrolled for further evaluation and follow-up.

Exclusion Criteria

Patients presenting with second-trimester pregnancy loss, ectopic pregnancies, or those with inadequate tissue samples that precluded a definitive histopathological diagnosis were excluded from the study.

Clinical and Ultrasonographic Assessment

Detailed clinical evaluation was performed for all patients, including documentation of demographic characteristics, obstetric history, presenting symptoms, and gestational age at presentation. Ultrasonographic findings were recorded and categorized as suggestive of molar pregnancy, consistent with early pregnancy loss, or inconclusive based on predefined imaging criteria.

Histopathological Examination

All products of conception were fixed in 10% buffered formalin and processed using standard paraffin embedding techniques. Tissue sections were stained with hematoxylin

and eosin (H&E) and examined microscopically. Diagnostic criteria for complete hydatidiform mole included diffuse villous hydrops, circumferential trophoblastic hyperplasia, and absence of fetal tissue. Partial hydatidiform mole was diagnosed based on the presence of scalloped villi, focal trophoblastic hyperplasia, cistern formation, and occasional fetal tissue. Invasive mole was identified by the presence of trophoblastic invasion into the myometrium.

β -hCG Monitoring

Serum β -hCG levels were measured pre-evacuation, 48 hours following evacuation, and subsequently monitored on a weekly basis until normalization. The development of gestational trophoblastic neoplasia was diagnosed according to the International Federation of Gynecology and Obstetrics (FIGO) criteria.

Statistical Analysis

The collected data were summarized using descriptive statistics in the form of frequencies and percentages. Concordance between clinical and ultrasonographic diagnoses with histopathological findings was assessed descriptively to evaluate diagnostic accuracy.

RESULTS

Out of the total 55 patients included in the study, the majority belonged to the 20-30-year age group, accounting for 31 patients (56.36%). Adolescents aged less than 20 years constituted 4 patients (7.27%) of the study population. Vaginal bleeding was the most common presenting symptom, observed in 47 patients (85.45%). Abdominal pain was reported by 25 patients (45.45%), while hyperemesis was present in 14 patients (25.45%). Passage of vesicles was noted in 6 patients (10.9%) (Table 1).

Table 1: Distribution of Clinical Symptoms among Patients (n = 55)

Clinical Symptom	Number of Patients (n)	Percentage (%)
Vaginal bleeding	47	85.45
Abdominal pain	25	45.45
Hyperemesis	14	25.45
Passage of vesicles	6	10.9

On ultrasonographic evaluation, a heterogeneous echogenic intrauterine mass was the most frequently observed finding, seen in 31 patients (56.36%). A classic “snowstorm”

appearance suggestive of molar pregnancy was identified in 17 patients (30.90%), while an early pregnancy loss-like appearance was noted in 7 patients (12.72%) (Table 2).

Table 2: Distribution of Ultrasonographic Findings (n = 55)

Ultrasonographic Finding	Number of Patients (n)	Percentage (%)
Classic “snowstorm” appearance	17	30.90
Heterogeneous echogenic mass	31	56.36
EPL-like appearance	7	12.72

Histopathological examination revealed that partial hydatidiform mole (PHM) was the most common diagnosis, observed in 29 cases (52.72%). Complete hydatidiform

mole (CHM) was identified in 24 cases (43.63%), while invasive mole was diagnosed in 2 cases (3.63%) (Table 3).

Table 3: Distribution of Histopathological Diagnosis (n = 55)

Histopathological Diagnosis	Number of Cases (n)	Percentage (%)
PHM	29	52.72
CHM	24	43.63
Invasive Mole	2	3.63

Pre-evacuation serum β -hCG levels between 100,000 and 1,000,000 IU/mL were observed in 29 patients (52.72%), while levels greater than 1,000,000 IU/mL were noted in 2 patients (3.63%) (Table 4).

Table 4: Distribution of Pre-evacuation Serum β -hCG Levels (n = 55)

Serum β -hCG Level (IU/mL)	Number of Patients (n)	Percentage (%)
100,000-1,000,000	29	52.72
> 1,000,000	2	3.63

Gestational trophoblastic neoplasia (GTN) developed in 4 patients (7.27%) during follow-up. All affected patients were successfully treated with single-agent methotrexate chemotherapy, with favorable clinical outcomes.

First-Trimester EPL Cohort (n = 255)

Among the 255 patients included in the first-trimester early pregnancy loss (EPL) cohort, none of the cases were clinically or ultrasonographically suspected to have a molar pregnancy at the time of initial evaluation. Histopathological examination of the products of conception identified molar pathology in 5 specimens

(1.96%) among the EPL cohort (n = 255). Of these, complete hydatidiform mole (CHM) was diagnosed in 2 cases (0.78%), while partial hydatidiform mole (PHM) was detected in 3 cases (1.18%). This corresponds to approximately one occult molar pregnancy detected for every 51 abortion specimens submitted for histopathological examination in the EPL cohort. All five patients underwent serial β -hCG surveillance during follow-up, which facilitated early detection and intervention, thereby preventing progression to gestational trophoblastic neoplasia (GTN).

Table 5: Histopathological Detection of Molar Pathology in EPL Cohort (n = 255)

Histopathological Diagnosis	Number of Cases (n)	Percentage (%)
CHM	2	0.78
PHM	3	1.18
Total Molar Pathology	5	1.96

DISCUSSION

Early pregnancy loss (EPL) remains one of the most common complications of pregnancy, and the majority of cases are clinically attributed to chromosomal abnormalities without further pathological confirmation. However, the possibility of underlying gestational trophoblastic disease (GTD), particularly partial hydatidiform mole (PHM), is often underestimated due to its nonspecific clinical and ultrasonographic presentation [6]. The present study highlights the diagnostic limitations of clinical and ultrasonographic evaluation alone and reinforces the role of routine histopathological examination (HPE) of products of conception (POC) in detecting occult molar pregnancies.

In the GTD cohort of this study, the most commonly affected age group was 20-30 years (56.36%). Ngan et al. in a study reported that the incidence of GTD increases with advancing years of age [9]. Although advanced maternal age is a recognized risk factor, these findings suggest that GTD can frequently occur in otherwise low-risk reproductive age groups, making reliance on demographic risk stratification inadequate for screening.

Vaginal bleeding was the most common presenting complaint in the present study (85.45%), followed by abdominal pain and hyperemesis. These findings are in agreement with several studies, where abnormal vaginal

bleeding was observed as the most common symptom in patients with molar pregnancy [9-12]. However, these symptoms are nonspecific and frequently overlap with clinical manifestations of EPL, thereby limiting their diagnostic utility.

Ultrasonographic evaluation demonstrated a heterogeneous echogenic intrauterine mass in 56.36% of cases, while the classic “snowstorm” appearance was observed in only 30.90% of patients. This is consistent with findings reported by Kirk et al. in a prospective study, which demonstrated that the sensitivity of ultrasonography in diagnosing PHM during early gestation is limited due to the absence of characteristic sonographic features [13]. Several other studies concur with the limitation of USG to detect PHM during early gestation [14,15]. Moreover, Braga et al. in a study reported that partial moles are frequently misdiagnosed as missed abortions on ultrasonography due to overlapping imaging characteristics [16]. In our study, 12.72% of GTD cases exhibited an EPL-like appearance on ultrasonography, further emphasizing the risk of missed diagnosis when imaging is used in isolation.

Histopathological examination in our study revealed PHM as the predominant subtype (52.72%), followed by CHM (43.63%). Similar distributions have been described by Ngan et al. in an epidemiological study, where PHM

constituted a higher proportion of molar pregnancies diagnosed following evaluation of first-trimester abortion specimens^[9]. This trend may be attributed to the increasing use of early ultrasonography, leading to earlier evacuation of pregnancies before classical clinical features of CHM become apparent.

A key finding of the present study was the detection of occult molar pathology in 5 out of 255 EPL specimens (1.96%), corresponding to approximately one occult mole per 51 abortion specimens. Ohayi et al. reported that routine histopathological analysis of products of conception identified hydatidiform moles in about 8.4% of cases and that a proportion of these were missed by clinical and ultrasound evaluation^[2]. Similarly studies demonstrated that a significant proportion of PHM cases are clinically unsuspected prior to histopathological evaluation^[17].

Importantly, none of the EPL cases in the present study were clinically or ultrasonographically suspected to have molar pregnancy at presentation. This observation is in concordance with several findings where the majority of PHM cases were diagnosed incidentally on histopathological examination following presumed spontaneous abortion^[17,18]. Failure to detect such cases may result in the absence of post-evacuation β -hCG surveillance, thereby increasing the risk of progression to gestational trophoblastic neoplasia (GTN).

All five patients with occult molar pathology in the present study underwent serial β -hCG monitoring following histopathological diagnosis, and none developed GTN during follow-up. Early initiation of surveillance likely contributed to favorable outcomes. Similar benefits of routine post-evacuation monitoring have been emphasized in several studies, which demonstrated that early detection of persistent trophoblastic disease significantly improves treatment outcomes and reduces the risk of metastatic progression^[9,19].

This study has certain limitations that should be acknowledged. Being a single-centre study, the findings may not be fully generalizable to other populations or healthcare settings. Immunohistochemical analysis was not performed, which may have aided in more accurate differentiation between partial hydatidiform mole and non-molar hydropic abortus in selected cases. Additionally, the duration of follow-up was limited, which may have precluded the detection of late progression to gestational trophoblastic neoplasia in some patients.

CONCLUSION

Taken together, these findings underscore the clinical importance of routine histopathological examination of POC in all first-trimester pregnancy losses. In resource-limited settings, where routine β -hCG follow-up may not be universally implemented, failure to identify occult molar pregnancies may delay GTN diagnosis and adversely affect patient outcomes. Therefore, incorporation of routine HPE into the management protocol for EPL may serve as a cost-effective strategy for early detection of GTD and prevention of subsequent neoplastic transformation.

Conflict of Interest

The authors declare no conflict of interest.

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