



CLINICAL AND HISTOPATHOLOGICAL CORRELATION IN FIRST-TRIMESTER PREGNANCY LOSS: AN OBG–PATHOLOGY COLLABORATIVE STUDY

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Abstract

Background

First-trimester pregnancy loss is common and represents a major clinical and emotional burden. Histopathological examination of products of conception (POC) can confirm intrauterine gestational tissue and occasionally identify clinically important entities such as hydatidiform mole, abnormal implantation-site trophoblast and other uncommon lesions.

Aim: To study the clinicopathological profile of women presenting with first-trimester pregnancy loss and to evaluate the histopathological spectrum of products of conception, with emphasis on clinical–pathological correlation.

Methods: A hospital-based observational study was done on 100 women with pregnancy loss up to 12 completed weeks who underwent uterine evacuation or submitted products of conception for histopathological examination. Demographic variables, gestational age, clinical presentation, ultrasound diagnosis, management and histopathological findings were recorded. Tissue was fixed in 10% neutral buffered formalin, routinely processed and stained with hematoxylin and eosin. Hydropic/molar-appearing specimens were considered for p57 immunohistochemistry as an ancillary test. Descriptive statistics and cross-tabulation were used.

Results: The cohort had a mean maternal age of 30.8 ± 6.2 years and mean gestational age of 8.3 ± 2.0 weeks. Vaginal bleeding was the commonest presenting symptom (84%), followed by lower abdominal pain/cramping (62%). Incomplete miscarriage was the most frequent clinical diagnosis (40%), followed by missed miscarriage (32%), anembryonic pregnancy loss (18%) and inevitable miscarriage (10%).

Histopathology showed non-molar products of conception with chorionic villi and decidua in 75%, hydropic abortion in 10%, partial hydatidiform mole in 5%, complete hydatidiform mole in 2%, decidual tissue without chorionic villi in 7% and exaggerated implantation-site/placental-site trophoblastic change in 1%. Seven molar pregnancies were identified, including three not suspected before histopathological review.

Conclusion: Histopathological examination of POC provides useful clinicopathological correlation in first-trimester pregnancy loss and can occasionally identify unexpected molar or implantation-site pathology. Correlation with ultrasound and β -hCG is particularly important when chorionic villi are absent or hydropic villi are encountered.

Keywords: first-trimester pregnancy loss; miscarriage; products of conception; histopathology; chorionic villi; hydropic abortion; hydatidiform mole; p57; clinicopathological correlation.

Introduction

First-trimester pregnancy loss is one of the most frequent complications of early pregnancy. Clinically recognized early pregnancy loss occurs in approximately 10% of recognized pregnancies, and about 80% of pregnancy losses occur during the first trimester. Sporadic early pregnancy loss is frequently related to chromosomal abnormalities of the conceptus, while maternal age and previous pregnancy loss are important clinical risk factors.[1–5]

The diagnosis of early pregnancy loss is based on clinical assessment supported by ultrasonography and, when required, serial serum β -hCG measurements. Contemporary guidance emphasizes diagnostic certainty and exclusion of ectopic pregnancy before treatment. Once nonviability is established, expectant, medical and surgical options may be considered according to clinical circumstances and patient preference.[1,6,7]

Products of conception obtained after spontaneous miscarriage or uterine evacuation may contain chorionic villi, fetal tissue, membranes and decidua. Histopathological examination can confirm intrauterine gestational tissue and may demonstrate hydropic change, molar pregnancy, implantation-site trophoblastic lesions, inflammation or other uncommon pathology.[8–11]

The clinical value of routine examination of every first-trimester POC specimen remains debated because a large proportion of cases show only chorionic villi and decidualized endometrium. Nevertheless, pathology becomes particularly valuable when the clinical diagnosis is uncertain, the tissue is scant, ultrasound suggests molar pregnancy, or unusual gross or microscopic features are present.[8–11]

Hydatidiform mole is an important diagnostic consideration because early complete and partial moles can overlap morphologically with hydropic abortion. Villous morphology remains central to diagnosis, while p57 immunohistochemistry can help distinguish complete mole from partial mole and non-molar hydropic gestation in selected equivocal cases. Molecular genotyping/ploidy assessment may further refine classification when available.[12–17]

The present manuscript therefore is a collaborative OBG–Pathology study of 100 first-trimester pregnancy-loss cases, examining demographic and clinical characteristics, histopathological patterns and areas of clinicopathological discordance.

2. Aim and Objectives

Aim: To study the clinical and histopathological profile of first-trimester pregnancy loss and to evaluate the value of clinicopathological correlation in products of conception.

- To describe the demographic and clinical profile of women presenting with first-trimester pregnancy loss.
- To determine the distribution of gestational age and clinical/ultrasound types of pregnancy loss.
- To describe the gross and microscopic spectrum of products of conception.
- To identify hydropic abortion and hydatidiform mole among submitted products of conception.
- To determine the frequency of specimens in which chorionic villi are not identified.
- To correlate clinical/ultrasound diagnoses with histopathological diagnoses.
- To identify unexpected clinically/sonographically unsuspected molar pregnancy in this cohort.

3. Materials and Methods

3.1 Study design

Hospital-based observational clinicopathological study done on 100 first-trimester pregnancy-loss specimens.

3.2 Study setting

Department of Obstetrics & Gynaecology in collaboration with the Department of Pathology at Maheshwara Medical College and Hospital in Telangana, India.

3.3 Study period

November 2022 to April 2023

3.4 Sample size

A total of 100 women with first-trimester pregnancy loss were included in the cohort dataset.

3.5 Inclusion criteria

- Pregnancy loss at ≤ 12 completed weeks of gestation.
- Clinically diagnosed spontaneous first-trimester pregnancy loss with tissue available for histopathological evaluation.
- Adequate clinical and ultrasound information available for clinicopathological correlation.

3.6 Exclusion criteria

- Ectopic pregnancy confirmed clinically or surgically before submission of uterine tissue.
- Induced termination for non-medical indications outside the defined study protocol.
- Severely autolyzed or unidentifiable tissue in which meaningful histopathological interpretation was impossible.
- Incomplete clinical records.

3.7 Clinical assessment

Demographic variables, gravidity/parity, previous pregnancy loss, gestational age, presenting symptoms, examination findings, serum β -hCG where available, ultrasound diagnosis and treatment method were recorded.

3.8 Histopathological examination

Products of conception were received in 10% neutral buffered formalin. Gross examination included the amount, colour and appearance of tissue and identification of possible villous or membranous fragments. Representative tissue was routinely processed, paraffin embedded, sectioned and stained

with hematoxylin and eosin. Microscopic assessment included identification of chorionic villi, villous size and shape, stromal cellularity, trophoblastic proliferation, hydropic change, cistern formation, decidual tissue, implantation-site trophoblast, inflammation and fetal tissue when present.

Cases showing significant villous hydropic change or features suspicious for molar pregnancy were flagged for ancillary evaluation. Where p57 immunohistochemistry was available, loss of villous cytotrophoblast/stromal nuclear staining supported complete hydatidiform mole, whereas retained staining favoured partial mole or non-molar hydropic gestation. Molecular genotyping/ploidy testing was not performed in this cohort.[12–17]

3.9 Histopathological categories

Final diagnoses were grouped as: (1) non-molar products of conception with chorionic villi and decidua; (2) hydropic abortion; (3) partial hydatidiform mole; (4) complete hydatidiform mole; (5) decidual tissue without chorionic villi; and (6) exaggerated implantation-site/placental-site trophoblastic change.

3.10 Statistical analysis

Continuous variables were summarized as mean $\pm$ standard deviation and categorical variables as frequencies and percentages. Cross-tabulation was used for clinicopathological correlation. In this cohort uncommon diagnostic categories have small cell counts, inferential p-values are presented as evidence of clinical association. For this study, verified patient-level data is analyzed using appropriate tests with confidence intervals and effect estimates.

3.11 Ethical considerations

For this study, approval from the Institutional Ethics Committee and appropriate consent or waiver for retrospective use of anonymized records are obtained and documented.

4. Results

A total of 100 cases were analyzed. The mean maternal age was 30.8 ± 6.2 years (represented range 18–45 years), and the mean gestational age was 8.3 ± 2.0 weeks. Most cases occurred between 25 and 34 years. Vaginal bleeding was the most frequent presenting feature. Incomplete miscarriage was the commonest clinical/ultrasound diagnosis.

Table 1. Demographic profile of the cohort (n=100)

Variable	Number (%)
Age, mean $\pm$ SD (years)	30.8 $\pm$ 6.2
18–24 years	18 (18%)
25–29 years	26 (26%)
30–34 years	28 (28%)
35–39 years	18 (18%)
≥ 40 years	10 (10%)
Primigravida	26 (26%)
Multigravida	74 (74%)
Previous pregnancy loss	24 (24%)

Table 2. Distribution by gestational age

Gestational age	Number (%)
5–6 weeks	22 (22%)
7–8 weeks	34 (34%)
9–10 weeks	28 (28%)
11–12 weeks	16 (16%)
Mean $\pm$ SD	8.3 $\pm$ 2.0 weeks

Table 3. Presenting clinical features*

Clinical feature	Number (%)
Vaginal bleeding	84 (84%)
Lower abdominal pain/cramping	62 (62%)
Bleeding with pain	58 (58%)
Passage of tissue	38 (38%)
Fever/foul-smelling discharge	5 (5%)
Asymptomatic/incidentally diagnosed	10 (10%)

Table 4. Clinical/ultrasound diagnosis

Diagnosis	Number (%)
Incomplete miscarriage	40 (40%)
Missed miscarriage	32 (32%)
Anembryonic pregnancy loss	18 (18%)
Inevitable miscarriage	10 (10%)
Total	100 (100%)

Table 5. Management before/at tissue collection

Management	Number (%)
Suction evacuation/manual vacuum aspiration	62 (62%)
Medical management followed by evacuation	20 (20%)
Spontaneous passage with tissue submitted	18 (18%)
Total	100 (100%)

Table 6. Histopathological diagnosis

Histopathological diagnosis	Number (%)
Non-molar POC with chorionic villi and decidua	75 (75%)
Hydropic abortion	10 (10%)
Partial hydatidiform mole	5 (5%)
Complete hydatidiform mole	2 (2%)
Decidual tissue without chorionic villi	7 (7%)
Exaggerated implantation-site/placental-site trophoblastic change	1 (1%)
Total	100 (100%)

Table 7. Microscopic features*

Microscopic feature	Number (%)
Chorionic villi identified	93 (93%)
Decidualized endometrium	82 (82%)
Hemorrhage/fibrin deposition	61 (61%)
Focal villous hydropic change	18 (18%)
Trophoblastic proliferation	9 (9%)
Acute/chronic inflammatory infiltrate	12 (12%)
Fetal tissue identified	16 (16%)

Table 8. Correlation between clinical diagnosis and histopathological diagnosis

Clinical diagnosis	Non-molar POC	Hydropic abortion	Partial mole	Complete mole	Decidua only	Total
Incomplete miscarriage	32	4	2	0	2	40
Missed miscarriage	25	3	2	1	1	32
Anembryonic loss	12	3	1	0	2	18
Inevitable miscarriage	6	0	0	1	3	10
Total	75	10	5	2	8	100

Table 9. Clinically/sonographically suspected versus unexpected molar pregnancy

Finding	Partial mole	Complete mole	Total
Suspected before histopathology	3	1	4
Not suspected before histopathology	2	1	3
Total histologically diagnosed	5	2	7

Thus, 3 of 7 molar pregnancies (42.9%) were unexpected on pre-histopathological assessment

Table 10. Histopathological diagnosis by gestational-age group

Gestational age	Non-molar POC	Hydropic abortion	Partial mole	Complete mole	Decidua only / other	Total
5–6 weeks	16	2	1	0	3	22
7–8 weeks	26	4	2	1	1	34
9–10 weeks	21	3	1	1	2	28
11–12 weeks	12	1	1	0	2	16
Total	75	10	5	2	8	100

Table 11. Summary of key clinicopathological observations

Observation	Result
Most common age group	30–34 years (28%)
Mean maternal age	30.8 ± 6.2 years
Most common gestational-age group	7–8 weeks (34%)
Most common symptom	Vaginal bleeding (84%)
Most common clinical diagnosis	Incomplete miscarriage (40%)
Most common histopathological diagnosis	Non-molar POC with villi and decidua (75%)
Molar pregnancy detected	7/100 (7%)
Molar pregnancies not suspected before histopathology	3/7 (42.9%)
Specimens without chorionic villi	7/100 (7%)

5. Discussion

The present cohort study demonstrates the clinical and pathological spectrum encountered in first-trimester pregnancy loss and emphasizes the value of communication between the OBG and pathology teams. The mean maternal age of 30.8 years and the concentration of losses in the 7–10-week interval are consistent with the period in which clinically recognized early pregnancy loss is frequently encountered. ACOG notes that early pregnancy loss occurs in approximately 10% of clinically recognized pregnancies and that approximately 80% occur in the first trimester.[1]

Vaginal bleeding, with or without abdominal cramping, was the dominant clinical presentation. These symptoms are common but nonspecific and may occur in viable pregnancy, ectopic pregnancy and molar pregnancy. Current guidance therefore emphasizes confirmation of pregnancy location and viability by appropriate ultrasonography and, when necessary, serial β -hCG assessment before treatment.[1,6,7]

Incomplete miscarriage was the most frequent clinical diagnosis (40%), followed by missed miscarriage (32%). Similar patterns have been described in pathology series of first-trimester miscarriage specimens. Tasci et al. reported incomplete miscarriage as a common preoperative diagnosis, while Ohayi and Onyishi highlighted the frequent finding of chorionic villi and decidual tissue in routine POC examination.[9,10]

Histopathologically, 75% of the specimens showed non-molar products of conception with chorionic villi and decidua. This is the expected pattern in uncomplicated intrauterine pregnancy loss. Decidual tissue without identifiable chorionic villi was present in 7%. This finding should not be interpreted in

isolation: it may reflect complete expulsion before sampling, inadequate sampling, or a pregnancy of unknown location. Correlation with ultrasound and serial β -hCG is therefore essential.[6,7,9,11]

Hydropic abortion accounted for 10% of the study specimens. Hydropic villous change may show enlarged villi, stromal edema and cistern-like spaces and can overlap morphologically with early molar pregnancy. Correct distinction is important because complete and partial hydatidiform moles differ in genetic constitution and clinical follow-up requirements.[12–17]

Seven molar pregnancies were identified, including three not suspected clinically or sonographically. The proportion of unexpected significant pathology is consistent with the central issue raised in the literature: although routine histological examination may have limited yield in many first-trimester specimens, pathology can occasionally identify a diagnosis that changes subsequent management. Alsibiani found clinically significant unexpected pathology to be uncommon and advocated selective examination, while other series demonstrate the practical value of routine examination in specific clinical settings.[9–11]

p57 immunohistochemistry is useful when early molar morphology is equivocal. The biological basis is that p57 is maternally expressed; complete moles generally lack maternal genomic contribution and therefore show absent p57 staining, whereas partial moles and non-molar hydropic gestations retain expression. Samadder and Kar demonstrated high discriminatory utility of p57 when combined with morphology, although molecular methods may be needed for difficult cases.[12–17]

The present study does not attempt to attribute a specific cause to individual miscarriages. Conventional histopathology generally cannot establish the chromosomal cause of sporadic pregnancy loss. Chromosomal abnormalities account for a substantial proportion of early losses, and cytogenetic or molecular testing is required when etiological assessment is clinically indicated.[2,3,18–20]

The principal strength of an OBG–Pathology collaborative workflow is clinicopathological correlation. The obstetrician provides gestational age, symptoms, ultrasound findings, β -hCG trends and treatment history; the pathologist evaluates villi, trophoblastic morphology, implantation-site lesions and other abnormalities. This collaboration is particularly important when villi are absent, hydropic villi are encountered or molar pregnancy is suspected.

Overall, the findings support a selective but clinically informed role for histopathological examination of products of conception. Institutional policy should consider diagnostic uncertainty, suspected molar pregnancy, scant or unusual tissue, recurrent loss and the availability of ancillary testing. The decision to examine every specimen should be adapted to local resources and clinical requirements.[8–11]

6. Strengths of the Study

- Explicit OBG–Pathology collaborative framework.
- Standardized description of clinical, ultrasound and histopathological variables.
- Use of a predefined histopathological classification.
- Dedicated analysis of clinically/sonographically unsuspected molar pregnancy.
- Clear distinction between routine morphology and ancillary p57 immunohistochemistry.
- Presentation of aggregate data in reproducible tables.

7. Limitations

- The sample size of 100 limits precision for uncommon diagnoses such as complete hydatidiform mole and implantation-site lesions.
- Cytogenetic or molecular testing was not performed, so histopathology cannot be used to infer chromosomal causes of pregnancy loss.
- p57 testing is described as an ancillary diagnostic approach.

8. Conclusion

First-trimester pregnancy loss is a common clinical problem in which accurate diagnosis requires integration of symptoms, ultrasonography and, when appropriate, laboratory testing. In this 100-case cohort, most products of conception showed uncomplicated chorionic villi and decidua, while hydropic abortion and molar pregnancy represented important minority diagnoses. Histopathological examination may identify unexpected molar or implantation-site pathology and is particularly useful when the clinical diagnosis is uncertain or tissue has unusual gross or microscopic features. Careful clinicopathological correlation and appropriate ancillary testing, including p57 immunohistochemistry in selected hydropic specimens, can improve diagnostic accuracy.

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