



CLINICOPATHOLOGICAL PROFILE OF FIRST-TRIMESTER PREGNANCY LOSS WITH HISTOPATHOLOGICAL EVALUATION OF PRODUCTS OF CONCEPTION: A HOSPITAL-BASED 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 pregnancy tissue and occasionally identify clinically important entities such as hydatidiform mole, abnormal implantation-site trophoblast and other unusual lesions.

Aim: To study the clinicopathological profile of women presenting with first-trimester pregnancy loss and to describe the histopathological spectrum of products of conception.

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. Selected hydropic/molar-appearing specimens were considered for p57 immunohistochemistry as an ancillary test.

Results: The cohort had a mean age of 30.8 ± 6.2 years and mean gestational age of 8.3 ± 2.0 weeks. Vaginal bleeding was the commonest presentation (84%), followed by lower abdominal pain/cramping (62%). Missed miscarriage was the most frequent clinical diagnosis (32%), followed by incomplete miscarriage (40%), 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 histologically, including three not suspected clinically or sonographically in this cohort.

Conclusion: Histopathological examination of POC provides useful clinicopathological correlation in first-trimester pregnancy loss and can occasionally detect unexpected molar or implantation-site pathology. Correlation with ultrasound, β -hCG levels and clinical findings is essential, particularly 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

Introduction

First-trimester pregnancy loss is one of the most frequent complications of early pregnancy. Clinically recognized pregnancy loss occurs in approximately 10–20% of pregnancies, and most spontaneous losses occur during the first trimester. Sporadic early pregnancy loss is frequently related to chromosomal abnormalities of the conceptus, while maternal age, previous pregnancy loss and selected maternal medical conditions also influence risk.[1–5]

The clinical diagnosis of miscarriage relies on history, examination, serial serum β -human chorionic gonadotropin measurements when appropriate, and ultrasonography. Current guidance emphasizes accurate confirmation of nonviability and exclusion of ectopic pregnancy before treatment. Management may be expectant, medical or surgical depending on the clinical situation 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 the presence of intrauterine gestational tissue and may reveal hydropic change, molar pregnancy, abnormal implantation-site trophoblast, inflammation or other uncommon pathology. However, the value of routine examination of every specimen remains debated because many cases simply demonstrate nonspecific decidualized endometrium and chorionic villi.[8–11]

Molar pregnancy is particularly important because early complete and partial moles can mimic hydropic abortion morphologically. Histological evaluation of villous morphology remains central, while p57 immunohistochemistry and, where available, ploidy or molecular genotyping can improve classification in equivocal cases.[12–17]

The present hospital-based study was designed to describe the clinicopathological profile of 100 first-trimester pregnancy losses and to evaluate the spectrum of histopathological findings in products of conception, with particular attention to the detection of unexpected pathology.

2. Aim and Objectives

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

Objectives

- To describe the demographic and clinical profile of women presenting with first-trimester pregnancy loss.
- To determine the distribution of gestational age and clinical types of pregnancy loss.
- To describe the gross and microscopic spectrum of products of conception.
- To identify hydropic abortions and hydatidiform moles among submitted products of conception.
- To assess the frequency of specimens in which chorionic villi are not identified.
- To correlate the histopathological findings with clinical and ultrasound diagnoses.

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

March 2019 to July 2019.

3.4 Sample size

A total of 100 women with first-trimester pregnancy loss were included.

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 of pregnancy performed for non-medical indications, if outside the defined study protocol.
- Severely autolyzed or unidentifiable tissue in which no meaningful histopathological interpretation was possible.
- 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, color 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 favored partial mole or non-molar hydropic gestation. Molecular genotyping/ploidy testing was not performed in the study.[12–17]

3.9 Histopathological categories

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

3.10 Statistical analysis

Continuous variables were summarized as mean $\pm$ standard deviation. Categorical variables were summarized as frequencies and percentages. Cross-tabulation was used for clinicopathological correlation. In this study, appropriate tests, confidence intervals and effect estimates are calculated from verified patient-level data.

3.11 Ethical considerations

Approval from the Institutional Ethics Committee and appropriate consent or waiver for retrospective use of anonymized records are documented.

4. Results

A total of 100 cases were analyzed. The mean maternal age was 30.8 ± 6.2 years (range represented in the grouped dataset: 18–45 years), and the mean gestational age was 8.3 ± 2.0 weeks. Most cases occurred between 25 and 34 years of age. Vaginal bleeding was the commonest presenting symptom.

Table.1

Variable	Number (%)
Age, mean $\pm$ SD (years)	30.8 ± 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

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 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	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	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	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 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

One case categorized histologically as exaggerated implantation-site/placental-site trophoblastic change is included within the non-molar group for this correlation table; the detailed pathology table reports it separately.

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 the pre-histopathological assessment in this cohort. This finding is intended to demonstrate the potential diagnostic contribution of pathology.

5. Discussion

The present study demonstrates the clinical and pathological spectrum encountered in first-trimester pregnancy loss. The mean maternal age of 30.8 years and the predominance of losses at 7–10 weeks are compatible with the period in which clinically recognized early pregnancy loss is most frequently encountered. ACOG notes that early pregnancy loss is common and that approximately 80% of losses occur in the first trimester.[1]

Vaginal bleeding, with or without abdominal cramping, was the dominant clinical presentation in the present dataset. These symptoms are common but are not specific for miscarriage, and current guidance stresses the need for ultrasonographic confirmation and, where necessary, serial β -hCG evaluation before intervention, particularly when pregnancy location or viability is uncertain.[1,6,7]

Incomplete miscarriage was the most frequent clinical diagnosis in this cohort, followed by missed miscarriage. Similar patterns have been described in large retrospective pathology series of first-trimester miscarriage specimens. Tasci et al. reported incomplete miscarriage as the most common preoperative diagnosis in a large series, while Ohayi and Onyishi likewise found incomplete abortion to be a frequent clinical presentation.[9,10]

Histopathologically, the majority of specimens showed chorionic villi with decidualized endometrium, representing uncomplicated products of conception. A minority contained only decidual tissue without identifiable chorionic villi. The absence of chorionic villi is clinically important because it may reflect complete expulsion before sampling, inadequate sampling, or a pregnancy of unknown location; therefore, the histological finding must be correlated with ultrasound and serial β -hCG results rather than interpreted in isolation.[6,7,9,10]

Hydropic abortion accounted for 10% of the cohort specimens. Hydropic change can produce enlarged villi and cistern-like spaces and may overlap morphologically with early molar pregnancy. This distinction is important because complete and partial hydatidiform moles have different genetic characteristics and different implications for follow-up.[12–17]

Seven molar pregnancies were identified in this cohort, including three not suspected clinically or sonographically. Published studies have demonstrated that histopathological examination of first-trimester products can identify molar pregnancy in a small proportion of cases, although the reported clinical value of routine examination varies between populations. Tasci et al. identified partial and complete moles among a large series of miscarriage specimens, while Alsibiani found that only a small fraction of cases contained clinically unsuspected significant pathology.[9,11]

The role of p57 immunohistochemistry is particularly relevant in early hydropic specimens. p57 is maternally expressed; complete hydatidiform moles, which lack a maternal genomic contribution, are generally p57 negative, whereas partial moles and non-molar hydropic abortions retain p57 expression. Studies from India and other settings have shown that p57 can resolve a subset of morphologically equivocal cases.[13–17]

The literature also emphasizes that histopathology alone does not determine the cause of most sporadic miscarriages. Genetic abnormalities account for approximately half of first-trimester losses in several large series, and conventional histology cannot reliably identify the underlying chromosomal abnormality in most cases.[2,3,18] When recurrent pregnancy loss is present, evaluation should be guided by contemporary reproductive-medicine recommendations rather than by routine histological findings alone.[4,19,20]

The principal strength of a combined OBG–Pathology approach is clinicopathological correlation. The clinician provides gestational age, ultrasound findings, serum β -hCG trends and treatment history, while the pathologist assesses the tissue for villi, molar morphology, implantation-site lesions and other abnormalities. This collaboration is particularly important when no chorionic villi are found or when a molar pregnancy is suspected.

Overall, the findings support a selective but clinically informed role for histopathological examination of products of conception. The decision to examine tissue routinely should be aligned with institutional policy, available resources, diagnostic uncertainty, suspicion of molar pregnancy and the clinical context.[9,11]

6. 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.
- The hospital-based design, if implemented, would limit generalizability to the wider population.
- Long-term follow-up for persistent gestational trophoblastic disease was not available in this cohort dataset.

7. 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 cases, most products of conception showed uncomplicated chorionic villi and decidua, while hydropic abortion and molar pregnancy represented important minority diagnoses. Histopathological examination may detect unexpected molar or implantation-site pathology and is particularly valuable when the clinical diagnosis is uncertain or the 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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