

# Histopathological evaluation of products of conception in sporadic and recurrent abortions

Original  
Article

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## ABSTRACT

**Background and study aims:** Fetal histopathology testing is an essential and common part of care for women experiencing miscarriage in the early stages of pregnancy. The study is being carried out to find out the prevalence of chronic histiocytic intervillitis among sporadic & recurrent miscarriage, as well as to evaluate the histological characteristics of products of conception in both types of miscarriage.

**Materials and Methods:** This was a cross-sectional study had been conducted at Women Health Hospital of Assiut University. A total of 300 women were recruited.

**Results:** Histopathological diagnosis in the current study was product of conception, no product of conception, partial mole and complete mole in 245 (81.7%), 45 (15%), 8 (2.7%) and 2 (0.70%) patients, respectively.

**Conclusion:** The prevalence of CHIV in the current study was rare. So, the need for histopathological evaluation of product of conception for CHIV is controversial. Multiple centers studies with cost analysis are warranted to assess the benefit of this issue.

**Key Words:** Conception, histopathological, recurrent abortion, sporadic.

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## INTRODUCTION

A miscarriage is considered early if it occurs within twelve weeks of pregnancy. Further tests, such as repeated evaluations of chorionic gonadotropin concentration ( $\beta$ -HCG) and imaging examinations - ultrasonography, are used to diagnose this condition in about ten to 15 percent of all pregnancies<sup>[1]</sup>.

Miscarriages are classified as either "complete" or "incomplete" based on clinical presentation and ultrasonographic findings. A miscarriage is considered "incomplete" when the echo of residual tissues in the uterine cavity is greater than ten mm on ultrasonography & is accompanied by clinical symptoms like vaginal bleeding & abdominal pain<sup>[2]</sup>.

When the gestational sac includes the embryo with a crown-rump length of more than seven mm but embryonic cardiac activity is not visible, this is referred to as a retained product of conception<sup>[3]</sup>.

When a gestational sac larger than 25 mm in diameter is seen in the uterine cavity on ultrasonography, it is considered to be empty and a diagnosis of an empty gestational sac made<sup>[3]</sup>.

Care for individuals with early pregnancy failure often includes histopathological investigation of products of conception<sup>[4]</sup>.

The study aimed to find out the prevalence of chronic histiocytic intervillitis between sporadic and recurrent miscarriage by analyzing the histological findings of products of conception in each.

## PATIENTS AND METHODS

The cross-sectional study was conducted onat Women Health Hospital of Assiut University. A total of 300 patients were recruited.

### **Inclusion criteria:**

All patients with gestational age below 24 weeks and needed surgical evacuation after being diagnosed as missed and incomplete abortion spontaneously. Following a vaginal examination, trans vaginal ultrasonography and serum BHCG (if needed) were used to confirm the diagnosis.

**Exclusion criteria:**

Complete miscarriage, cases that managed with expectant or medical management, induced abortion, partial mole and complete molar pregnancy.

**Sample Size Calculation:**

A total coverage sampling technique was applied in the current study, where all patients who were present with sporadic or recurrent abortion during the study period were approached to be included in this study. A total of 300 patients were recruited.

**Operational design:**

All study participants were provided with an explanation of the technique. Before beginning the trial, all patients provided written consent and were counseled about the benefits of the research.

**Methods:****Every Patient was submitted to:****Data collection:**

All ladies who were found to be trial participants had their medical records checked. Information such as the patient's name, age, residence, medical and obstetric history, and gestational age at the time of the intended procedure. Age at menarche, menstrual disturbance, related symptoms, dysmenorrhea, obstetric history, including parity and mode of delivery, present history: of chronic diseases and medication, past history of HTN, DM, history of allergy, family history of similar condition or diabetes, to any medication, and surgical history of operation, laparoscopic interference.

**Examination:** General examination: Evaluation of vital signs & weight, height measurement (BMI). Abdominal and local clinical examination: Evaluation of fundal level, surgical scar, gestational age, pain, mass, or stiffness, and clinically apparent abdominal or pelvic illness.

**Investigations:**

**Laboratory:** Blood group and Rh typing complete blood count (CBC), coagulation profile to detect bleeding tendency and random blood sugar.

Patients' pregnancies are confirmed by an ultrasound. Then, all tissues obtained during evacuation were submitted for histopathological evaluation. All specimens were fixed in 10 percent formalin for twenty-four hours at room temperature, embedded in paraffin wax, and sectioned at five  $\mu\text{m}$  for conventional histopathological evaluation.

To examine the histopathological alterations, hematoxylin-eosin (H&E)-stained and Olympus microscope-observed tissue sections were used.

**Research outcome measures:****Primary Outcome Measure:**

The outcome of the histopathological examination of the analysis of abortion products was classified into groups according to the result: products of conception, no products of conception, partial mole, and complete mole.

**Secondary Outcome Measures:**

Explore the pathologic findings associated with specific etiologies as chronic histiocytic intervillitis.

**Ethical Consideration:**

Approved from the Committee of Medical Ethics of Faculty of Medicine, Assiut University (IRB17101115). Each individual in the study gave verbal agreement after receiving adequate information. At every stage of the investigation, confidentiality and individual privacy were maintained.

**Data management and Statistical Analysis:**

In order to tabulate and statistically analyze the collected data, we used SPSS (Statistical Program for the Social Sciences) version 26.0, Microsoft Excel 2016, and MedCalc program software version (19.1).

**RESULTS**

Mean age of the enrolled women was 28.90 years with vary from 18 and 44 years old. A total of 97 (32.3%) patients had normal body mass index and only two women were obese class-II. It was found that 165 (55%) and 36 (12%) patients were overweight and obese class-I respectively. Majority (76.4%) of the women was multiparous while only 71 (23.6%) was nulliparous.

The current miscarriage occurred in 218 (72.7%) patients in the first trimester while in 82 (27.3%) patients had abortion during the second trimester. As regard type of the current abortion; it was missed embryonic sac, missed anembryonic pregnancy and incomplete abortion in 102 (34%), 30 (10%) and 168 (56%) patients, respectively. All patients were managed with surgical intervention.

Histopathological diagnosis in the current study was product of conception, no product of conception, partial mole and complete mole in 245 (81.7%), 45 (15%), 8 (2.7%) and 2 (0.70%) patients, respectively.

In case of the diagnosis “products of conception”; deciduitis, endometritis, acute villitis, increased perivillitis fibrin and hydropic abortus were present in 114 (46.5%), 22 (9%), 27 (11%), 23 (9.4%) and 11 (4.5%) patients, respectively. CHIV was present in only women.

In case of the diagnosis “no products of conception”; deciduitis, endometritis and Arias-Stella reaction were present in 40 (88.9%), 5 (11.2%) and 11 (24.4%) patients, respectively. CHIV was absent in all women with diagnosis of “no product of conception”

It was found that histopathological evaluation of POC and no-POC showed no significant differences between nulliparous and multiparous women ( $p > 0.05$ ).

It was found that histopathological evaluation of POC and no-POC showed no significant differences between sporadic and recurrent abortion ( $p > 0.05$ ).

It was found that histopathological evaluation of POC and no-POC showed no significant differences between 1<sup>st</sup> and 2<sup>nd</sup> trimester abortion ( $p > 0.05$ ).

**Table 1:** Baseline data of the studied group

	N= 300
Age (years)	28.90 ± 5.34
Range	18-44
Class of body mass index	
Normal BMI	97 (32.3%)
Overweight	165 (55%)
Obese class-I	36 (12%)
Obesity class-II	2 (0.7%)
Parity	
Nulliparous	76 (25.3%)
Multiparous	224 (74.7%)
Previous abortion	
Sporadic	264 (88%)
Recurrent	36 (12%)
First trimester previous abortion	187 (62.3%)
Second trimester previous abortion	272 (90.7%)

Data expressed as frequency (percentage), mean (SD), range. N: number

**Table 2:** Characteristics of the current abortion in the studied patients

	N= 300
Timing	
First trimester	218 (72.7%)
Second trimester	82 (27.3%)
Type of abortion	
Missed embryonic pregnancy	102 (34%)
Missed anembryonic sac	30 (10%)
Incomplete abortion	168 (56%)
Surgical management	300 (100%)

Data expressed as frequency (percentage). N: number

**Table 3:** Histopathological findings in case of products of conception based on parity

	Nulliparous (n= 68)	Multiparous (n=177)	<i>P value</i>
Deciduitis	30 (44.1%)	84 (47.6%)	0.53
Endometritis	5 (7.4%)	17 (9.6%)	0.46
Acute villitis	10 (14.7%)	17 (9.6%)	0.34
Increased perivillous fibrin	4 (5.9%)	19 (10.7%)	0.23
Hydropic abortus	4 (5.9%)	7 (3.9%)	0.31
CHIV	0	1 (0.50%)	0.73

Data expressed as frequency (percentage). N: number; CHIV: chronic histiocytic intervillitis

**Table 4:** Histopathological findings in case of no-products of conception based on parity

	Nulliparous (n= 8)	Multiparous (n= 37)	<i>P value</i>
Deciduitis	6 (75%)	34 (91.9%)	0.21
Endometritis	0	5 (13.5%)	0.35
Arias-Stella reaction	3 (37.5%)	8 (21.6%)	0.29

Data expressed as frequency (percentage). N: number

**Table 5:** Histopathological findings of products of conception based on type of abortion

	Recurrent (n= 27)	Sporadic (n= 218)	<i>P value</i>
Deciduitis	14 (51.8%)	100 (45.9%)	0.12
Endometritis	0	22 (10.1%)	0.07
Acute villitis	2 (7.4%)	25 (11.5%)	0.43
Increased perivillous fibrin	1 (3.7%)	22 (10.1%)	0.26
Hydropic abortus	3 (11.1%)	8 (36.7%)	0.05
CHIV	0	1 (0.50%)	0.69

Data expressed as frequency (percentage). N: number; CHIV: chronic histiocytic intervillitis

**Table 6:** Histopathological findings of products of conception based on timing of abortion

	1 <sup>st</sup> trimetric (n= 184)	2 <sup>nd</sup> trimetric (n= 61)	<i>P value</i>
Deciduitis	84 (45.7%)	30 (49.2%)	0.29
Endometritis	17 (9.2%)	5 (8.2%)	0.35
Acute villitis	16 (8.7%)	11 (18%)	0.19
Increased perivillous fibrin	18 (9.9%)	5 (8.2%)	0.31
Hydropic abortus	10 (5.4%)	1 (1.6%)	0.12
CHIV	0	1 (1.6%)	0.28

Data expressed as frequency (percentage). N: number; CHIV: chronic histiocytic intervillitis

**Table 7:** Histopathological finding of no-products of conception based on timing of abortion

	1 <sup>st</sup> trimetric (n= 34)	2 <sup>nd</sup> trimetric (n= 11)	<i>P value</i>
Deciduitis	30 (88.2%)	10 (90.9%)	0.64
Endometritis	4 (11.8%)	1 (9.1%)	0.65
Arias-Stella reaction	10 (29.4%)	1 (9.1%)	0.17

Data expressed as frequency (percentage). N: number

## DISCUSSION

There is no reliable data on the prevalence of CHIV or massive perivillous fibrin deposition in the context of miscarriage, but a small percentage of women with recurrent spontaneous abortion may show evidence of these histopathological diagnoses, which may affect future reproductive monitoring. This is because these conditions affect only about one in two hundred to one in two thousand pregnancies<sup>[5]</sup>.

Familial hydatidiform mole syndrome is an extremely rare condition characterized by recurrent, generally full hydatidiform moles of biparental instead of androgenetic origin, likely the result of dysregulation of imprinting. This disorder has been linked to repeated pregnancy losses<sup>[6]</sup>.

In the current trial, a total of 300 patients were recruited. All of them present with sporadic or recurrent abortion. The purpose of this study was to compare the results of histopathological examinations of fetuses lost to recurrent and sporadic miscarriage. Mean age of the enrolled patients was 28.90 years with range between 18 and 44 year's old.

Majority (88%) of patients had previous sporadic abortion while the other 36 (12%) patients had previous recurrent abortion. As regard the timing of the previous abortion; it occurred during 1<sup>st</sup> trimester and 2<sup>nd</sup> trimester in 187 (62.3%) and 272 (907%) patients, respectively.

Eighty-two (27.3%) patients had abortion during the second trimester. As regard type of the current abortion; it was missed embryonic pregnancy, missed anembryonic sac

and incomplete abortion in 102 (34%), 30 (10%) and 168 (56%) patients, respectively. All patients were managed with surgical intervention. According to the present results, Alsibiani SA 2014<sup>[6]</sup> analyzed data from 558 women who had been hospitalized to the hospital with the diagnosis of miscarriage in the 1<sup>st</sup> trimester. Their mean age was  $33.7 \pm 7.5$  years (range: 14 to 48 years) and mean parity was  $3.1 \pm 2$ .

In  $0.45 \pm 1.0$  of the cases, there was a previous miscarriage. On admission, the clinical diagnosis was incomplete miscarriage in 253 (45.3percent), missed miscarriage in 253 (45.3percent), blighted ovum in 28 (5.0%), query full miscarriage in fifteen (2.7percent), unavoidable miscarriage in six (1.1percent), and septic pregnancy in three (0.5percent) individuals<sup>[6]</sup>.

Histopathological diagnosis in the current study was product of conception, no product of conception, partial mole and complete mole in 245 (81.7%), 45 (15%), 8 (2.7%) and 2 (0.70%) patients, respectively.

Recently, According to a meta-analysis, approximately 1-third of complete hydatidiform moles & 2 -thirds of partial hydatidiform moles are not diagnosed on ultrasound in cases of missed miscarriage, histopathological investigation of all products of conception is essential for identifying molar changes in cases of early pregnancy failure. This is significant for the treatment of patients with full hydatidiform moles who have a higher risk of developing gestational trophoblastic neoplasia<sup>[7]</sup>.

In the current, in case of the diagnosis “products of conception”; deciduitis, endometritis, acute villitis, increased perivillitis fibrin and hydropic abortus were present in 114 (46.5%), 22 (9%), 27 (11%), 23 (9.4%) and 11 (4.5%) patients, respectively. CHIV was present in only one woman. Also, in case of the diagnosis “no products of conception”; deciduitis, endometritis and Arias-Stella reaction were present in 40 (88.9 %%%), 5 (11.2%) and 11 (24.4%) patients, respectively.

Chronic histiocytic intervillitis (CHIV) is uncommon. Maternal mononuclear cells have been found to infiltrate the intervillous space. Unknown incidence details exist. According to one study, the prevalence of miscarriages in the second and third trimesters was 0.6 per 1000 placentas and 9.6 per 1000 miscarriages overall<sup>[8]</sup>. Another trial indicated lesions in 4.4 percent of 1<sup>st</sup> trimester miscarriages<sup>[9]</sup>.

CHIV is usually related with intervillous & perivillous fibrinoid deposition at the materno-fetal interface, which anchors villi, and surrounding decidua. Labarrere *et al.*<sup>[10]</sup> first defined this pathological disease as extensive chronic intervillitis. CHIV is an unknown-pathogenesis placental lesion linked with reproductive loss at all gestational ages<sup>[11]</sup>.

Children with chronic histiocytic intervillitis in the placenta had a lower birth weight & shorter crown-to-heel length than children with only localized villitis in the placenta. CHIV has a significant recurrence incidence in subsequent pregnancies, ranging from 67 to 100 percent. There is a great probability of fetal loss during all trimesters of pregnancy. Although it is not possible to rule out the possibility of an unidentified placental infection, an immunological reason seems to be happening<sup>[10]</sup>.

In addition to confirming that CHIV is linked with increased rates of unfavorable pregnancy results, such as fetal death, IUGR, & premature delivery, a prior investigation identified relevant clinical, biochemical, and radiological findings in pregnancies with a histopathologic diagnosis of CHIV. Although none of these results frequently accompanied a diagnosis of CHIV & unfavorable pregnancy outcomes, they might assist physicians & women in response of an individual care plans for the control of subsequent pregnancies with the goal of improving results<sup>[12]</sup>.

Immunologically mediated flow of maternal histiocytes into the intervillous space is thought to be the 2rycause of placental insufficiency, which in turn leads to the degradation of syncytiotrophoblast cells, the accumulation of fibrin deposits within the syncytiotrophoblast lesions, and the subsequent compromise of maternal-fetal exchange<sup>[13]</sup>.

There was no long-term follow-up of the patients, and the sample size was rather small. To evaluate the impact of different histological findings on subsequent pregnancies, it is advised that such a research be conducted at many centers with a large number of patients, and that follow-up data be obtained. The cost-benefit of doing a histological examination of the fetus needs to be calculated, which necessitates a cost-benefit analysis.

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## CONCLUSION

The frequency of CHIV in the current study was rare. So, the need for histopathological evaluation of product of conception for CHIV is controversial. Multiple centers studies with cost analysis are warranted to assess the benefit of this issue. A histopathological analysis should be conducted if a preoperative diagnosis cannot be made, if fewer tissues than expected have been obtained, if an ultrasound demonstrates a molar pregnancy, if the women is at high risk for trophoblastic disease, or if inspection during surgery reveals unexpected pathology.

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## CONFLICT OF INTEREST

There are no conflicts of interests.

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