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RESEARCH ARTICLE

Assessment of Histopathological Features of the Placenta and Plasma Level of βHCG, Estrogen, and Progesterone in First-Trimester Spontaneous Miscarriage

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ABSTRACT

Miscarriage is a distressing complication with many fetal and maternal abnormalities. About 15% of pregnancies end in spontaneous miscarriages, and over 80% of these occur in the first 12 weeks of gestation. This research aims to evaluate the changes in the hormonal status in addition to determining the types and incidences of abnormalities in the decidua and chorionic villi of placentas that have been aborted. The peripheral blood samples were collected from twenty normal pregnant women as a control group and 30 aborted women. The obstetric characteristics results showed that the patients' mean maternal age was 25.73 ± 7.32 years compared with 25.5 ± 4.12 years in controls with no significant differences. Similarly, the two groups were comparable in gravida, parity, and history of abortion with no significant differences. The histopathological examination of the placenta from women who miscarried revealed that twenty cases (66.67%) showed hemorrhage, whereas 16 patients (53.33%) showed inflammation. Fifty percent of aborted placentas revealed necrosis, 6.67% had edema, 40% showed congested blood vessels, 13.33% had hydropic degeneration, and 13.33% showed partial hydatidiform mole. Only one case showed complete H. mole; 40% revealed fibrinoid deposition, 46.67% had fibrosis, and 16.67 illustrated hyalinization. The hormonal study showed highly significant differences between the study groups in the human chorionic gonadotropin, Estradiol, and progesterone hormones. We conclude that a comprehensive study that includes a histopathological examination of the placenta and other clinical investigations is essential for a better understanding of miscarriage.

Keywords: Estradiol, Histopathology, Human chorionic gonadotropin, Miscarriage, Placenta, Progesterone

Introduction

The most frequent pregnancy problem is a spontaneous miscarriage, which is a common gynecological emergency. The term "miscarriage" refers to the loss of a pregnancy before viability. Worldwide, it is estimated that 23 million miscarriages occur every year or 44 pregnancy losses every minute. About 15–20% of pregnancies end in spontaneous miscarriage, and over 80% of these happen in the first 12 weeks of gestation. The World Health Organization (WHO) classifies spontaneous miscarriage as the loss of a fetus within 22 weeks of pregnancy or the removal of a fetus (embryo) that weighs less than 500 g. Early miscarriage is the term used to describe miscarriages that happen before 12 weeks of pregnancy. On the other hand, miscarriages occurring between 12 and 20 weeks of gestation are referred to as late miscarriages.[1–4] Miscarriage is a distressing complication with many fetal and maternal abnormalities as its causes, including genetics in the form of ploidy and translocation in about 50% of cases; maternal factors

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include maternal infections, poisons, immunological, anatomical uterine abnormalities, cervical incompetence, hormonal imbalance, uncontrolled diabetes, and endocrine abnormalities as well. During the first trimester of pregnancy, most miscarriages occur, accounting for around 80% of unexpected fetal deaths. These miscarriages are often characterized by symptoms such as bleeding and discomfort, which can lead to significant maternal anxiety.[5–7]

Age and parity both closely correlate with the increase in miscarriages. Miscarriages increase with the number of pregnancies; in other words, both the number of children and the frequency of miscarriages are increased in grand multiparas.[8] The placenta, which contains tissues from both the mother and the fetus, is the site of exchange for nutrients, wastes, oxygen, and carbon dioxide. The trophoblast gives rise to the embryonic portion, the chorion, whereas the decidua basalis gives rise to the maternal portion. Mother blood in the decidua basalis lacunae exchanges with embryonic blood in the chorionic villi outside the embryo.[9]

Understanding the progression of fetal and placental development throughout gestation is necessary for evaluating the products of conception during the pre-viable phase. The cytotrophoblast and syncytiotrophoblast trophoblast types make up the placenta's villous compartment, or the lining surrounding the chorionic villi, and are necessary for exchanging gases and nutrients. Pregnancy problems may arise from abnormalities in the development of the fetus and placenta. Due to aneuploidy or environmental disturbance, abnormal fetal development can result in severe fetal abnormalities and pregnancy loss. Pathophysiology illustrates placental disease, focusing on the placenta's role in early pregnancy development, implantation, maturation, and vascularization. Physicians and scientists have been interested in the pathology of the placenta and conception for centuries. A pathologist examination of the placenta is required in situations of miscarriage, late intrauterine death, pre-eclampsia, growth limitation, infection, and fetal deformity.[10,11] The histopathology of first-trimester abortion products can help to diagnose diseases that are likely to recur in subsequent pregnancies or that explain unfavorable fetal outcomes, as well as provide essential details that are crucial for identifying the cause and guiding individuals experiencing early pregnancy failure.[12] Pregnancy-related complications are still complicated to treat if early detection of impending pathology allows for intervention and illness amelioration.[13]

In addition to mediating implantation and creating the interface for gas and nutrition exchange between the mother's and fetal's circulations, it also triggers the mother's recognition of her pregnancy, modifies the local immunological milieu, and modifies the mother's cardiovascular and metabolic processes by generating paracrine and endocrine hormones; it produces Estrogen(E2), Progesterone(P4), and β-human chorionic gonadotropin(βhCG), lactogen, relaxin, and other growth factors. Abnormalities in any one of these placental functions can be linked to a poor pregnancy outcome, such as intrauterine growth restriction (IUGR) and fetal or perinatal death, releasing the placenta as an endocrine organ.[14–16]

Human chorionic gonadotropin (βhCG) is a trophoblast hormone product that has been investigated extensively. This glycoprotein is essential during pregnancy because it prevents the corpus luteum from involution, which keeps the ovarian granulosa cells secreting progesterone. Because it might be among the first secreted products of the conceptus, it can be used as a diagnostic sign for pregnancy.[17] βhCG performs a variety of roles. In addition to stimulating the production of progesterone by corpus luteal cells, βhCG also increases angiogenesis in the uterine vasculature, fuses cytotrophoblast cells, and differentiates them into syncytiotrophoblast cells, blocks the mother's immune or macrophage response to foreign invaders in the placenta, which causes the uterus to grow in tandem with the fetus, inhibits myometrial contractions during pregnancy, stimulates the growth and differentiation of the umbilical cord, and alerts the endometrium to impending implantation.[18] It seems that if the levels of βhCG decrease during the initial stages of pregnancy, it could be an indication of a nonviable pregnancy, either a failed intrauterine pregnancy or an ectopic pregnancy.[19,20]

Progesterone is a 21-carbon steroid hormone that is produced by granulosa cells. Progesterone plays a crucial role in reproductive processes. During the first ten weeks of pregnancy, the corpus luteum produces most of the progesterone. Maintaining pregnancy and facilitating blastocyst nesting, it plays a role in the menstrual cycle, allowing the endometrial transition from a proliferative to a secretory stage and implantation.[21,22] Progesterone secretion may be insufficient in many cases of miscarriage; as a result, progestogens have been used in these circumstances, starting in the first trimester of pregnancy, to avoid spontaneous miscarriage.[23,24]

The hormone estrogen promotes endometrial hyperplasia, thickens the myometrium, increases blood flow, and strengthens the force of uterine contractions. Researchers indicate that estradiol has a significant role in maintaining early pregnancy. Serum estradiol level and gestational age had a favorable

correlation throughout the first 4–8 weeks of pregnancy.[25] Early in pregnancy, the estradiol level can assist in sustaining the corpus luteum and reflect the quality of the dominant follicle. Although numerous tissues can synthesize Estradiol from androgen and use it in a paracrine or intracrine manner, estrogen production is most generally thought of as an endocrine product of the ovary. It is present in many human tissues and cells, including ovarian granulosa cells, the placental syncytiotrophoblast, adipose and skin fibroblasts, bone, and the brain.[26] Compared to women who had a normal pregnancy, those who had an abortion had significantly lower serum estradiol levels.[27]

Materials and methods

During the study period from February 2022 to June 2023, 20 women with normal pregnancy were chosen as a control group for hormonal status, and 30 reproductive-aged women with different clinical types of spontaneous miscarriage before 12 weeks of gestation were evaluated as a second group. Those women were hospitalized due to vaginal bleeding and abdominal pain during the first trimester of their pregnancies. They were included in this prospective study after informed consent and approval of the study protocol by the institute's hospital ethical committee. Data were collected from women included in this study by direct questionnaire, which included Gravida, parity, gestational age, and history of pregnancy miscarriages. An obstetric history of preeclampsia, diabetes, and endocrine disorders were excluded. The ages of the women were different, ranging from 16 to 45 years. Products of conception were collected from aborted women as they were admitted for uterine evacuation at the women's emergency department in Fatema AL-Zahraa Hospital in Baghdad province.

The evacuation of the uterus was performed by curettage. Placental tissues were fixed in 10% formalin, embedded in paraffin blocks, cut at 5μ sections, and stained by hematoxylin and eosin. Blood samples of 3 ml were taken from women in this study for serum βhCG, Progesterone, and Estradiol assay. The samples were collected without anticoagulant in gel tubes. The serum was separated by centrifugation and stored at 2–8 ˚C until hormonal assay. The assay principle combines an enzyme immunoassay competition method with final fluorescent detection. The approval number of the ethics committee was 9559 in 2022 from the Baghdad Health Department.

Statistical analysis

Statistical analyses were performed using SPSS software version 25.0 (SPSS, Chicago). Continuous data were subjected to a normality test (Shapiro-Wilk test); data with normal distribution were presented as mean and standard deviation and analyzed with a student t-test. Data with non-normal distribution were presented as median and range and analyzed with the Mann-Whitney U test. Categorical variables were expressed as numbers and percentages and analyzed with the Chi-square test and Fisher's exact test. The receiver operating characteristic curve (ROC) was used to evaluate different hormones in predicting pregnancy loss. A p-value less than 0.001 was considered to indicate a statistically highly significant difference.

Results and discussion

Demographic and obstetric characteristics of the study population

The mean maternal age of the first trimester patients was 25.73±7.32 years compared with 25.5±4.12 years in controls, with no significant differences. Similarly, the two groups were comparable in gravida, parity, and history of abortion with no significant differences, as seen in Table 1. According to one study, risk factors for the 15% of pregnancies that result in a miscarriage include age at conception.[28]

Table 1. Demographic and reproductive characteristics of women with first-trimester pregnancy loss and control.

Variables		Patients (n = 30)	Controls (n = 20)	p-value
Maternal age, years	Mean ± SD	25.73 ± 7.32	25.5 ± 4.12	0.925
	Range	16–40	18–40	
Gravida	1–2	14(64.67%)	3(30%)	0.500
	3–4	7(23.33%)	2(20%)	
	>4	9(30%)	5(50%)	
Parity	1–2	20(66.67%)	7(70%)	0.868
	3–4	5(16.67%)	2(20%)	
	>4	5(16.67%)	1(10%)	
Abortin	0–2	26(86.67%)	8(80%)	0.629
	≥2	4(13.33%)	2(20%)	

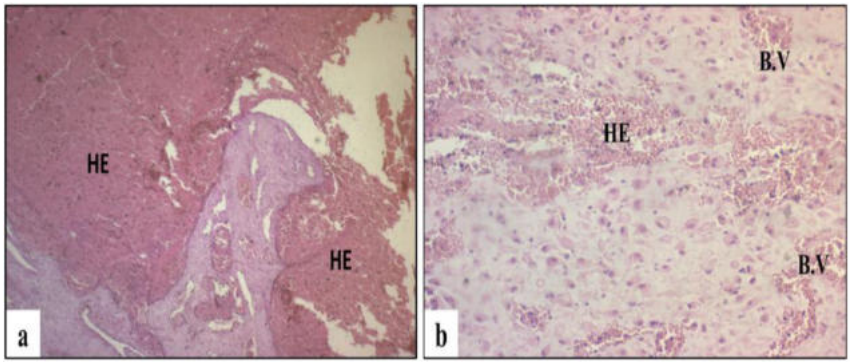

Fig. 1. Photomicrographs demonstrating placenta (decidua; maternal side) from first-trimester spontaneous miscarriage: a. Decidua showed severe peridecidual hemorrhage (HE), 100X. b. Decidua with hemorrhage (HE) and congested blood vessels (B.V), 200X, Hematoxylin and eosin (H&E) stain.

A mother's age above 35, placenta previa, excessive gravidity, multiparity, prior cesarean births, and past curettage are risk factors for the development of abnormal placentation.[29]

A study revealed that women between the ages of 25 and 29 had the lowest miscarriage risk (9.8%), while women over the age of forty-five had the highest risk (53.6%). The absolute lowest risk was at age 27 (9.5%). The risk of pregnancy was 15.8% for mothers under 20 years of age.[30] Maternal age and the risk of spontaneous abortion have been found to have a non-linear relationship in certain studies. The risk is slightly higher in the youngest women and rises substantially in those over 35 years.[31] A study by Andersen et al. found that high maternal age, independent of parity or the number of prior miscarriages, was a significant risk factor for spontaneous abortion.[32]

Histopathological findings

Abortions that occur spontaneously are very prevalent. The initial pathologic assessment is done to identify a molar pregnancy and determine if pregnancy tissue is present or absent. Determining the aetiology of complications during pregnancy, fetal mortality, abortion, and morbidity is aided by histopathological analysis of the placenta with clinical consequences, which aids in family planning and neonatal risk assessment.[33] Various placental histopathologic abnormalities were found in the first-trimester group. Understanding how the normal placenta develops is crucial to understanding the context of abnormal changes. Many major pregnancy issues are associated with insufficient trophoblast invasion, even though they might not present symptoms until later in pregnancy.[34]

During the research period, the total number of miscarriage cases was thirty in the first-trimester miscarriage; their pathological examination was as follows:

Table 2. Pathological changes in the placenta of women with first-trimester miscarriages.

Pathological change	Frequency	Percent %
Hemorrhage	20	66.67
Inflammation	16	53.33
Necrosis	15	50
Fibrosis	14	46.67
Congested blood vessels	12	40
Fibrinoid necrosis	12	40
Hyalinization	5	16.67
Partial H mole	4	13.33
Hydropic change	4	13.33
Edema	2	6.67
Complete H mole	1	3.33

Table 2 revealed that twenty cases (66.68%) of first-trimester miscarriage showed hemorrhage in decidua, as seen in Fig. 1a, b. In cases of spontaneous miscarriage, hemorrhage in the decidua and villi is often seen. The impairment of the placenta-decidual interface causes the early and vast beginning of maternal blood flow. Two things happen when maternal blood excessively enters the intervillous spaces: the villous tissue is directly affected mechanically, and oxidative stress increases. The main cause of bleeding during the first trimester of pregnancy is decidual hemorrhage, which is linked to partial spiral artery remodeling and decidual inflammation later in pregnancy.[35,36] In the current study, 16 patients (53.33%) of the specimens showed inflammation Table 2, Fig. 2. Acute or chronic placental inflammation can cause miscarriage and other unfavorable pregnancy outcomes. Placental dysfunction and adverse pregnancy outcomes have been linked to acute inflammation of the placenta, which can be infectious or non-infectious. A poor pregnancy outcome is associated with chronic inflammatory lesions of the placenta, which are defined by the infiltration of the

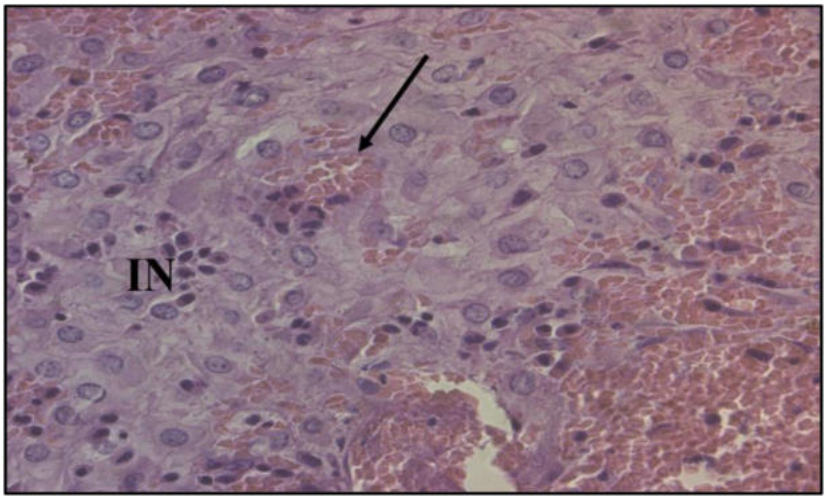

Fig. 2. Photomicrographs demonstrating placenta (decidua; maternal side) from first-trimester spontaneous miscarriage revealed thinly walled vessels congested with blood (arrow) and inflammation with mainly neutrophils and lymphocytes (IN), 400X.

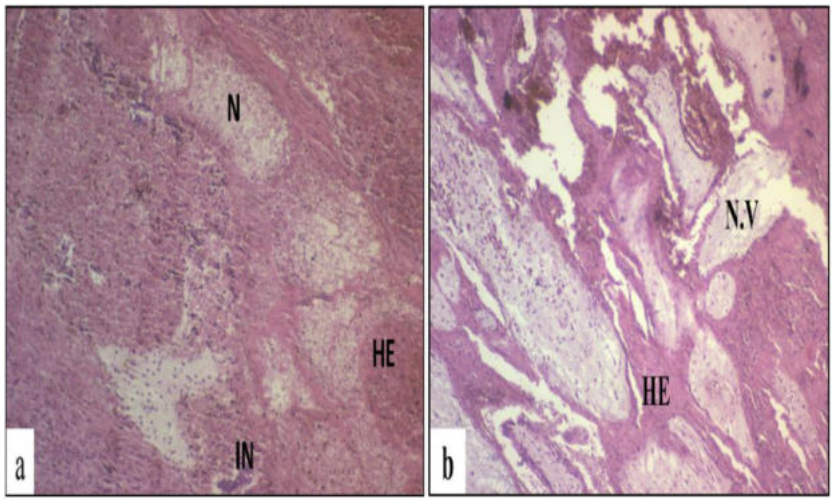

Fig. 3. Photomicrographs demonstrating placenta a. Decidua (maternal side) from first-trimester spontaneous miscarriage revealed necrosis (N), hemorrhage (HE), and inflammation (IN),100X. b. Chorionic villi (fetal side) showed necrotic villi (N.V.) and hemorrhage in between. 100X. Hematoxylin and eosin (H&E) stain.

placenta by different immune cells such as lymphocytes, plasma cells, and macrophages; they can also be immune-related (maternal anti-fetal rejection) or products of bacterial, viral, or parasite infections. The three main lesions are chronic deciduitis (affecting the decidua basalis), chronic chorioamnionitis (affecting the chorioamniotic membranes), and villitis (when the inflammatory process involves the villous tree).[37,38]

This study reported that fifty percent of placental specimens revealed necrosis Table 2, Fig. 3a, b. During necrosis, only ghost cells remain (necrotic cells without nuclei and a persisting membrane). Gradually, granulocyte infiltrates become more extensive and eventually predominant as karyorrhectic debris accumulates (nuclear debris from necrosis).[39] The placental specimens had 46.67% fibrosis Table 2, Fig. 4. The placental barrier between fetal and maternal blood thickens because of increased villous collagen and thickness of the sub-trophoblastic basement membrane, reducing the exchange of materials across the placenta. Hyalinization appeared in five cases of miscarriage, which is a pathological observation that can be made in a variety of pregnancy situations, such as hypertensive, diabetic, and normal pregnancies. Chronic inflammation, placental polyps, and fibrinoid necrosis are among the disorders linked to it. The avascular villi and necrotic tissue that are present during hyalinization are characteristic. Depending on the pregnancy condition, the placenta's

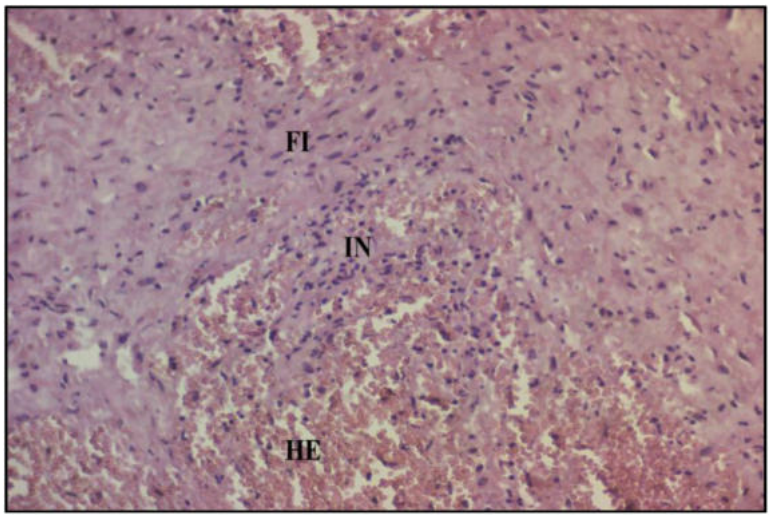

Fig. 4. Photomicrographs demonstrating placenta (decidua; maternal side) from first-trimester spontaneous miscarriage showed fibrotic change (FI), hemorrhage (HE), inflammation (IN), 200X. Hematoxylin and eosin (H&E) stain.

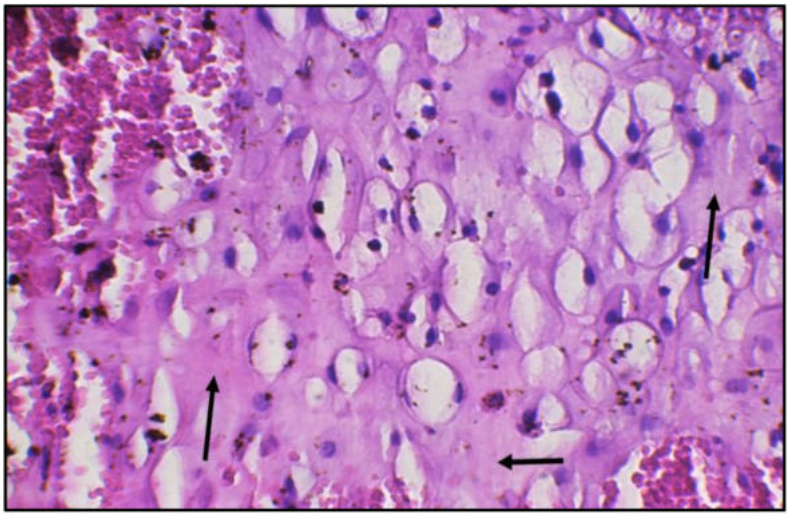

Fig. 5. Photomicrographs demonstrating placenta (decidua; maternal side) from first-trimester spontaneous miscarriage showed hyalinization (black arrow), 400X. Hematoxylin and eosin (H&E) stain.

level of hyalinization might change. Hyalinization of the placenta in the case of a miscarriage may be a sign of placental damage and may affect the course of the pregnancy,[40] Table 2, Fig. 5.

Our study showed that 40% of specimens had congested blood vessels, as seen in Table 2, Fig. 6; 40% of cases illustrated fibrinoid deposition, and 6.67% had edema, as shown in Table 2, Figs. 7 and 8. These cases of miscarriage are considered placental disorders that are caused by inadequate invasion of the endometrium by the cytotrophoblast and insufficient lumen filling. Anatomical evidence of improper placentation is present in around two-thirds of early pregnancy failures. This is linked to the lack of physiological alterations in most spiral arteries, resulting in a diminished vascular reaction in mothers during placentation. Whatever the reason for the miscarriage, too much maternal blood entering the intervillous space causes two things: it directly damages the villous tissue, causing it to become increasingly entangled, and it raises the amounts of lipid peroxides in the decidual and villous tissues, pathological oxidative stress is linked to abnormal placentation, immune disturbances, and placental dysfunction, and there is a clear association of oxidative stress with many pregnancy-specific disorders such as recurrent pregnancy loss (RPL), preeclampsia, fetal growth restriction (FGR) and fetal death.[35,41,42]

In addition, the results revealed that 4 cases showed hydropic degeneration. Hydropic change is

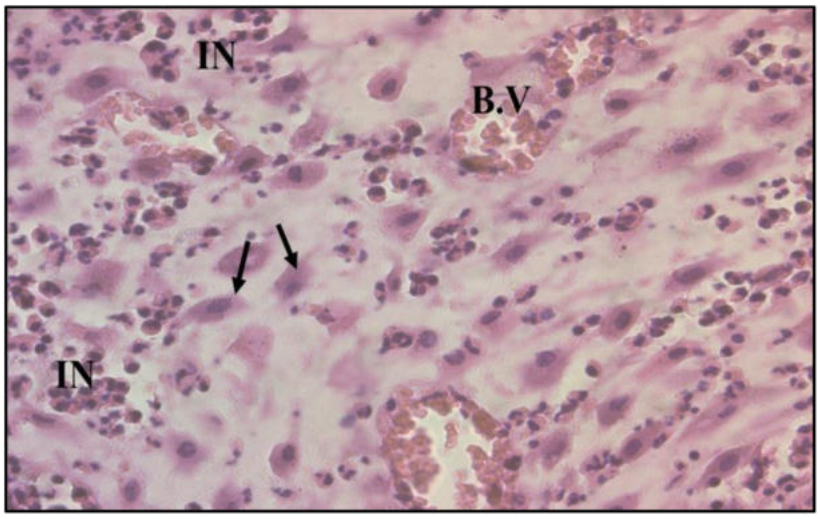

Fig. 6. Photomicrographs demonstrating placenta (decidua; maternal side) from first-trimester spontaneous miscarriage showed Degenerated decidual cells (arrows), heavy inflammatory cells (IN), congested blood vessels (B.V), 400X. Hematoxylin and eosin (H&E) stain.

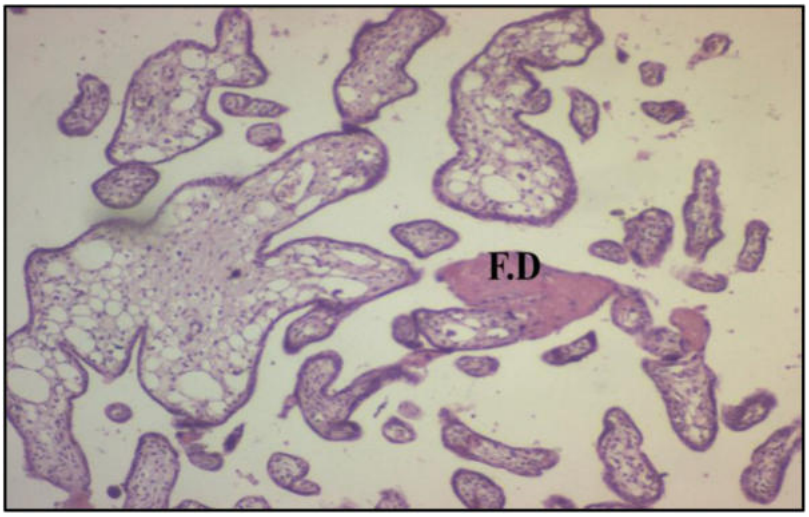

Fig. 7. Photomicrographs demonstrating placenta (chorionic villi; fetal side) from first-trimester spontaneous miscarriage showed fibrinoid deposition between villi, 100X. Hematoxylin and eosin (H&E) stain.

predominant in aborted specimens for unknown reasons. After fetal death, trophoblasts continue to transport water from the intervillous space into the villi, where an absent fetal circulation cannot remove it, thus causing the villi to enlarge. At about 6.5 weeks of menstrual age, villous vascularization occurs, so conceptuses will show villous capillaries and nucleated red blood cells and have fewer hydropic changes,[43] Table 2, Fig. 9. Our results also showed that 13.33% of the samples were of partial hydatidiform moles, as seen in Table 2, Fig. 10. In contrast, only one case showed a complete H. mole, Table 2, Fig. 11.

Gestational trophoblastic diseases are defined as the abnormal proliferation of trophoblastic cells. According to WHO, these disorders are divided into molar and non-molar lesions; molar lesions are divided into complete and partial hydatidiform moles.[43] A "mole" is a shapeless mass, and "hydatidiform" refers to a drop of water. The term "hydatidiform mole" refers to an abnormal placenta that has two characteristics: The chorionic villi undergo an enlarged, edematous, and hydropic alteration, eventually becoming vesicular, variable trophoblastic proliferation circumferentially. Molar pregnancy is most common before the age of 20 years and after the age of 40. For reasons that are now unknown, the frequency of hydatidiform moles varies worldwide; in Asia and Central America, the incidence is roughly ten times higher than in the United States. The

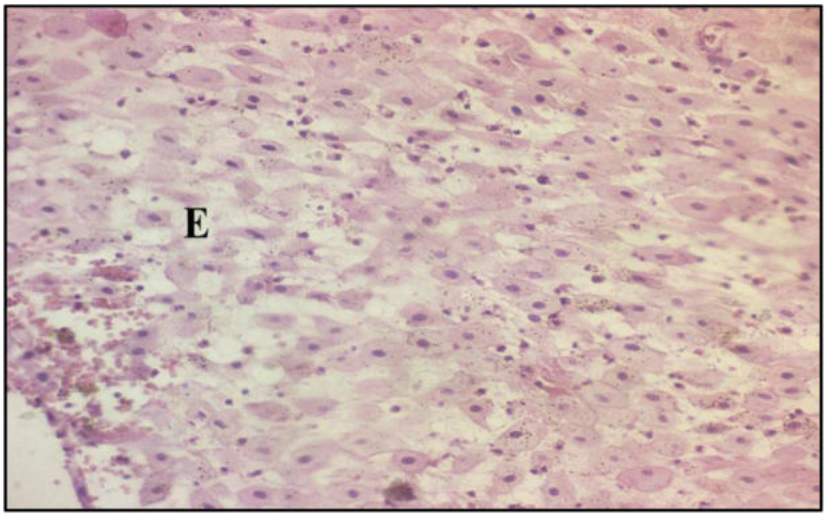

Fig. 8. Photomicrographs demonstrating placenta (decidua; maternal side) from first-trimester spontaneous miscarriage showed edema (E) 200X. Hematoxylin and eosin (H&E) stain.

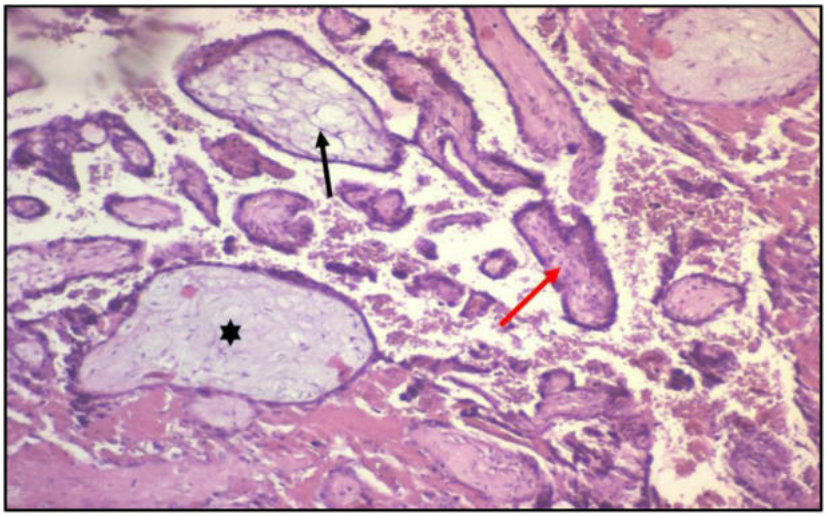

Fig. 9. Photomicrographs demonstrating placenta (chorionic villi; fetal side) from first-trimester spontaneous miscarriage showed Hydropic change of placenta, Syncytial knots increased, there is no cytotrophoblastic proliferation, a low number of fetal capillaries, villi are small in size some of them have hydropic change (black arrow) with myxoid stroma (star), others were fibrotic (red arrow), fibrinoid deposition between villi, 100X. Hematoxylin and eosin (H&E) stain.

incidence is higher among those from lower socioeconomic classes. Without a recognizable fetus or embryo, complete hydatidiform moles show early and uniform hydatid expansion of the villi, hyperplastic trophoblasts with variable degrees of atypia, and absent villous capillaries. Most complete moles (about 90% of them) are 46, XX, which result from haploid sperm duplication following egg fertilization (where the mother chromosomes are inactive). Due to two sperm fertilizing an empty ovum, 46, XY or 46, XX comprise the remaining 10% of complete moles (dispermy). Fetal tissue, chorionic villi with focal edema, scalloping, prominent stromal trophoblastic elements, a functional villous circulation, and localized trophoblastic hyperplasia with only mild atypia are all visible in partial hydatidiform moles. Most partial moles are triploid in the karyotype (often 69, XXY), which is the product of two sperm fertilizing an ovum that looks normal.[33,44,45]

Hormonal study

The results of the hormonal status in both study groups, as seen in Table 3, illustrate that the concentrations of the βhCG, Estradiol(E2), and Progesterone(P4) hormones were 10501.7 $\pm$ 17351.3

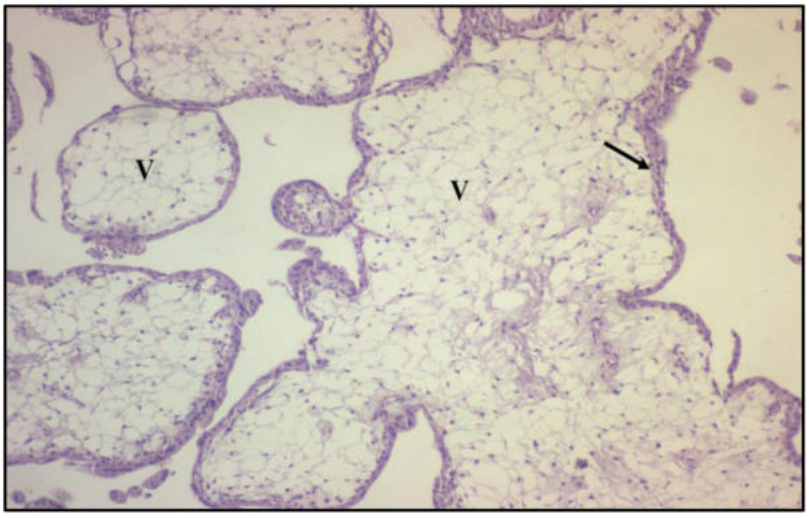

Fig. 10. Photomicrographs demonstrating placenta (chorionic villi; fetal side) from first-trimester spontaneous miscarriage showed Partial H. mole, Villi were enlarged hydropic with scalloped outlines, mild circumferential trophoblastic proliferation (arrow), 100X. Hematoxylin and eosin (H&E) stain.

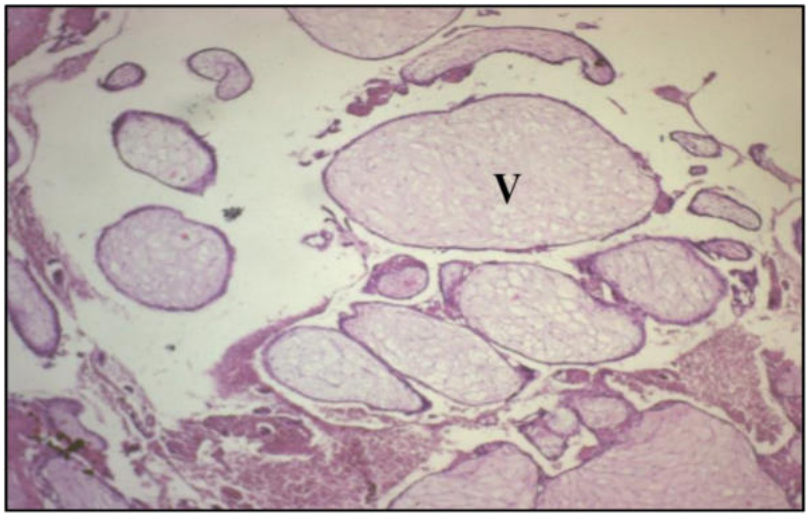

Fig. 11. Photomicrographs demonstrating placenta (chorionic villi; fetal side) from first-trimester spontaneous miscarriage: a. Complete H. mole, enlargement and rounding of hydropic villi with myxoid stroma, absence of fetal capillaries, moderate circumferential trophoblastic proliferation with atypia, 40X. Hematoxylin and eosin (H&E) stain.

Table 3. Hormonal profile of women with first-trimester pregnancy loss and control.

Variables		Patients (n = 30)	Controls (n = 20)	p-value
β hCG (mIU/ml)	Mean ± SD	10501.7 ± 17351.3	74033 ± 14073	<0.001
	Median	4570	760000	
	Range	50–77680	48840–92240	
E2 (pg/ml)	Mean ± SD	139.45 ± 224.19	3648.3 ± 2671.88	<0.001
	Median	72.1	3072	
	Range	28.5–951	732–9511	
P4 (ng/ml)	Mean ± SD	6.5 ± 7.29	60.26 ± 21.46	<0.001
	Median	4.3	64.55	
	Range	0.4–30.5	29.2–96.5	

SD: standard deviation; <0.001: highly significant.

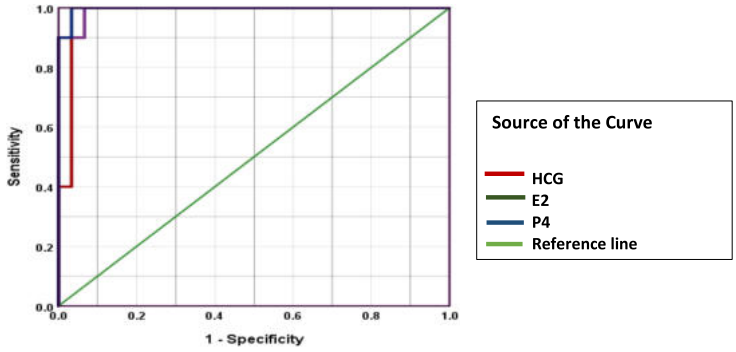

Fig. 12. Receiver operating characteristic curve for hCG, E2, and P4 predicting pregnancy loss in the first trimester.

(mIU/ml), 139.45 ± 224.19 (pg/ml), 6.5 ± 7.29 (ng/ml) respectively, in the first-trimester miscarriage group compared to the control group at 74033 ± 14073 (mIU/ml), 3648.3 ± 2671.88 (pg/ml), 60.26 ± 21.46(ng/ml). These results show highly significant differences in the three hormones between the study groups.

Predictive value of βhCG, E2, and P4 for pregnancy loss in the first trimester

The receiver operating characteristic curve was used to explore the predictive value of βhCG, E2, and P4 in predicting pregnancy loss in women in the first trimester. For βhCG, the area under the curve was 0.977, 95% CI = 0.991–1.0, p < 0.001. The sensitivity and specificity of the test at the cut-off value of βhCG = 53.500 mIU/ml were 97% and 100%, respectively. For E2, the AUC was 0.993, 95%CI = 0.976–1.00, p< 0.001. The sensitivity and specificity at a cut-off value of E2 = 1188 pg/ml were 90% and 100%, respectively. For P4, the AUC was 0.997, 95%CI=0.986-1.00, p< 0.001. The sensitivity and specificity at the cut-off value of P4 = 26 ng/ml were 100% and 97%, respectively, Fig. 12.

Our study showed a significant decrease in serum levels of βhCG, estradiol, and progesterone in the group of individuals who experienced a miscarriage. Prior research has also proved a decrease in the levels of these indicators, which suggests a poor outcome for pregnancy. Nevertheless, the precise significance of these variables in forecasting miscarriage remains unclear.[46,47] The abnormal secretion of some placental hormones during gestational disorders may be a response by the placenta and fetal membranes to unfavorable environmental conditions such as hypertension, hypoxia, infection, or fetal and placental abnormalities.[48] Reduced levels of human chorionic gonadotropin (βhCG) in the first trimester of pregnancy are linked to a higher likelihood of experiencing a miscarriage after the pregnancy has been clinically identified and may play an imperative role in the aetiology of spontaneous abortion. The mechanisms responsible for late first-trimester and second-trimester miscarriages may have been started as early as the first week of implantation.[49]

Progesterone is responsible for sustaining the initial stages of pregnancy and is primarily produced by the corpus luteum; later on, it is produced by the placenta.[50] Naturally occurring or luteal phase defect-induced insufficient production of progesterone and delayed growth of the endometrium during implantation or early pregnancy have been identified as potential causes of both sporadic and recurrent losses. The importance of progesterone during implantation is becoming more widely known. During this time, progesterone maintains decidualization, regulates uterine contractility, and strengthens the mother's immune system against the developing fetal semi-allograft. Therefore, a high serum progesterone level may offer protection against miscarriage early in pregnancy. On the other hand, a low serum progesterone level may raise the chance of a subsequent spontaneous miscarriage. Deterioration of placental transfer may lead to an insufficient supply of various bioactive factors, such as hormones, immunological compounds, and infection resistance, in addition to an inadequate supply of nutrition and oxygen support. The recent finding of significantly elevated rates of miscarriage in women with low progesterone levels, even with therapy, is a crucial issue to take into consideration when providing counselling and predicting pregnancy outcomes.[51] Deng et al. revealed that during the 5–6 and 7–9 weeks of pregnancy, the miscarriage group had decreased blood estradiol levels compared to the normal pregnancy group. Similarly, those experiencing miscarriage exhibited lower progesterone levels during the 7–9-week period of pregnancy.[25] Placental hormonal abnormality is a conspicuous condition that indicates dysfunction of the fetus and placenta. It occurs during the initial stages of pregnancy and continues to

worsen throughout the pregnancy, often leading to loss.[52]

Conclusion

This study demonstrates the importance of the histopathological examination of the placenta in cases of spontaneous miscarriage; most cases of miscarriage have abnormalities in both decidua and chorionic villi. Histopathological examination is a crucial implement for diagnosing molar pregnancy and providing insight into any maternal diseases that may influence the placenta. It also helps predict the fate of future pregnancies and determine the necessary interventions. βhCG, estradiol and progesterone levels can be used to predict the occurrence of miscarriage during the first trimester; measuring low levels of βhCG, estradiol and progesterone between 4–12 weeks of pregnancy can be utilized to forecast the occurrence of miscarriage more accurately in the first trimester.

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Authors' declaration

- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are ours. Furthermore, any Figures and images that are not ours have been included with the necessary permission for republication, which is attached to the manuscript.
- No animal studies are present in the manuscript.
- Author(s) signed on ethical consideration's.
- Ethical Clearance: The project was approved by the local ethical committee at University of University of Baghdad.

Authors' contribution statement

M. K. H. interpretations, proofreading, and writing. R. H. H. collected the samples, conducted data analysis, enrolled the results, wrote, and discussed.

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تقييم الخصائص النسيجية المرضية للمشيمة ومستوى هرمون موجهة الغدد التناسلية المشيمية البشرية والإستروجين والبروجسترون في بلازما الدم في حالات الإجهاض التلقائي في الثلث الأول من الحمل

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الخلاصة

الإجهاض هو أحد المضاعفات المؤلمة التي تصاحب العديد من تشوهات الجنين والأم. حوالي 15% من حالات الحمل تنتهي بالإجهاض التلقائي، وأكثر من 80% منها تحدث في الأسابيع الـ 12 الأولى من الحمل. يهدف هذا البحث إلى تقييم التغيرات في الحالة الهرمونية بالإضافة إلى تحديد أنواع وحالات التشوهات في الغشاء الساقط والزغابات المشيمية في المشيمات التي تم إجهاضها. تم جمع عينات الدم المحيطي من 20 امرأة حامل طبيعية كمجموعة مراقبة و30 امرأة مجهضة في الثلث الأول من الحمل. أظهرت نتائج الخصائص التوليدية أن متوسط عمر الأم لمرضى الأشهر الثلاثة الأولى كان 25.73 ± 7.32 سنة مقارنة بـ 25.5 ± 4.12 سنة في مجموعة المراقبة مع عدم وجود فروق ذات دلالة إحصائية. وبالمثل، فإن المجموعتان كانتا قابلتان للمقارنة في الحمل، والتكافؤ، وتاريخ الإجهاض مع عدم وجود فروق ذات دلالة إحصائية. كشف الفحص النسيجي المرضي للمشيمة من النساء المجهضات أن عشرين حالة (66.67٪) من حالات الإجهاض في الثلث الأول أظهرت نزيفًا في الغشاء الساقط، في حين أظهرت 16 مريضة (53.33٪) التهابًا. كما أظهرت خمسون بالمائة من المشيمات المجهضة نخرًا في المشيمة ، و6.67% منها وذمة، و40% أوعية دموية تخثرية، و13.33% تنكسًا مائيًا، و13.33% أظهرت كيساً مائياً جزئياً. في المقابل، أظهرت حالة واحدة فقط كيساً مائياً كاملاً؛ كشف 40% عن ترسب الفيبرينويد، و46.67% مصابون بالتليف، و16.67% مصابون بالتليف الزجاجي. أظهرت الدراسة الهرمونية عن وجود فروق ذات دلالة إحصائية كبيرة بين مجموعتا الدراسة في هرمونات موجهة الغدد التناسلية المشيمية البشرية (βhCG)، والإستراديول (E2)، والبروجستيرون (P4). نستنتج أن إجراء دراسة شاملة تتضمن الفحص النسيجي المرضي للمشيمة وغيرها من الفحوصات السريرية والمخبرية أمر ضروري لفهم أفضل للإجهاض. .

الكلمات المفتاحية: استراديول، علم ألامراض النسجي، هرمون الغدد التناسلية المشيمية البشرية، الإجهاض، المشيمة، البروجسترون.