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HOW BLEEDING SYNDROMES IN PREGNANCY AFFECT THE INCIDENCE OF ABORTION

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ABSTRACT

Hemorrhagic syndromes in the first half of pregnancy comprise potentially serious clinical conditions, including abortion, ectopic pregnancy and hydatidiform mole. Miscarriage, defined as termination of pregnancy before 20 weeks or with a fetal weight of less than 500 g, is the most common cause, with multifactorial etiologies such as genetic alterations and maternal factors. Ectopic pregnancy occurs when the embryo implants itself outside the uterine cavity, often in the fallopian tubes, and is associated with severe abdominal pain and the risk of rupture with bleeding. Hydatidiform mole, a gestational trophoblastic disease, is characterized by abnormal trophoblast proliferation and pathological placental development. Diagnosis is based on clinical history, ultrasound and beta-hCG levels. Management depends on the etiology and may include curettage, laparoscopy or chemotherapy in the case of hydatidiform mole. Early identification and appropriate treatment are essential to reduce maternal morbidity and mortality.

Keywords: Hemorrhage. Abortion. Ectopic Pregnancy. Hydatidiform Mole. Beta-hCG. Diagnosis. Treatment.

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INTRODUCTION

Hemorrhagic syndromes in the first half of pregnancy are one of the main causes of maternal morbidity and mortality in early pregnancy, requiring early and effective interventions (Cunningham et al., 2018).

Among the most frequent causes are abortion, ectopic pregnancy and hydatidiform mole, which have different clinical characteristics and outcomes. Miscarriage, defined as the spontaneous or induced termination of pregnancy before 20 weeks or with a fetal weight of less than 500 g, occurs in around 10-20% of clinically recognized pregnancies. The most common causes include fetal chromosomal abnormalities (50-60%), cervical insufficiency, infections and chronic maternal diseases. The clinical picture is often manifested by vaginal bleeding and abdominal pain, and differential diagnosis requires ultrasound and serum beta-hCG levels. Management includes expectant management in cases of complete abortion or interventions such as manual vacuum aspiration and curettage for incomplete abortions (Cunningham et al., 2018; WHO, 2021).

Ectopic pregnancy, characterized by implantation of the embryo outside the uterine cavity, represents 1-2% of all pregnancies and constitutes a medical emergency due to the risk of tubal rupture and severe bleeding. Risk factors include pelvic inflammatory disease, previous tubal surgery, endometriosis and the use of intrauterine devices. Diagnosis is based on a combination of transvaginal ultrasound and serum beta-hCG levels, especially when these are not compatible with an intrauterine pregnancy. Management varies according to the clinical presentation and may include expectant management in stable cases, administration of methotrexate in selected cases and surgical intervention (salpingostomy or salpingectomy) in situations of hemodynamic instability or tubal rupture (Practice Bulletin, 2018).

Hydatidiform mole is a form of gestational trophoblastic disease resulting from abnormal trophoblast proliferation. It can be classified as complete mola, which presents a diploid karyotype (46, XX or 46,XY) and absence of fetal tissue, or partial mola, with a triploid karyotype (69, XXX or 69,XXY) and presence of abnormal fetal tissue(Berkowitz & Goldstein, 2020).

Symptoms include vaginal bleeding, uterine enlargement disproportionate to gestational age and extremely high beta-hCG levels. Diagnostic confirmation is made by ultrasound, which often reveals a “snowstorm” appearance (Berkowitz & Goldstein, 2020).

Treatment consists of uterine evacuation by aspiration, followed by close monitoring of beta-hCG levels to detect possible cases of persistent trophoblastic disease or malignancy (Berkowitz & Goldstein, 2020; Grimes, 2016).

Although technological and therapeutic advances have improved the prognosis of hemorrhagic syndromes in the first half of pregnancy, challenges remain, especially in low- and middle-income countries. The lack of access to early diagnosis and appropriate interventions contributes significantly to the associated complications and maternal mortality. Measures such as expanding access to quality obstetric care, training health professionals and using evidence-based clinical guidelines are essential to reducing the impacts of these conditions (WHO, 2021).

OBJECTIVES

GENERAL OBJECTIVE

To analyze the main hemorrhagic syndromes in the first half of pregnancy, with an emphasis on miscarriage, ectopic pregnancy and hydatidiform mole, identifying their clinical characteristics, risk factors, diagnostic methods and therapeutic options, in order to contribute to improving the management of these conditions and reducing maternal complications.

SPECIFIC OBJECTIVES

- ✓ To review the scientific literature on the epidemiology, etiology and risk factors associated with miscarriage, ectopic pregnancy and hydatidiform mole.
- ✓ To identify the clinical and laboratory signs that differentiate these conditions in the context of hemorrhagic syndromes in the first half of pregnancy.
- ✓ Evaluate the most effective diagnostic tools, including laboratory and imaging tests.
- ✓ Describe contemporary therapeutic approaches, including conservative, pharmacological and surgical methods, and discuss their applicability in different clinical contexts.

METHODOLOGY

TYPE OF STUDY

This study consists of an integrative literature review, which aims to gather and synthesize the available scientific knowledge on hemorrhagic syndromes in the first half of pregnancy, including miscarriage, ectopic pregnancy and hydatidiform mole.

databases

The bibliographic search was carried out in the PubMed, SciELO and Medline databases, using combinations of descriptors in English and Portuguese, such as “abortion”, “ectopic pregnancy”, “hydatidiform mole”, “hemorrhagic syndromes in pregnancy” and “gestational trophoblastic disease”.

inclusion criteria

Articles published between 2015 and 2023 were selected, focusing on human studies, systematic reviews, clinical trials, and guidelines from recognized institutions. Publications in English, Portuguese and Spanish were included.

exclusion criteria

Articles with low clinical relevance, duplicate publications, studies based exclusively on animal models or with insufficient samples for generalization were excluded.

collection procedures

Articles were selected in stages, including reading titles, abstracts and then the full text. The data extracted was categorized according to the specific objectives: epidemiology, diagnosis, management and global challenges.

data analysis

The data was analyzed qualitatively, considering diagnostic and therapeutic advances, as well as the challenges encountered in low- and middle-income contexts. The synthesis of the information was structured to respond to the proposed objectives and highlight gaps in the literature.

limitations

It is recognized that the review may be limited by the heterogeneity of the studies included, especially in relation to regional and socioeconomic conditions that influence the management of hemorrhagic syndromes.

RESULTS AND DISCUSSION

Abortion, defined as the spontaneous termination of pregnancy before 20 weeks, is the most common cause of bleeding in the first half of pregnancy. Clinical signs include vaginal bleeding of varying intensity and colicky abdominal pain, which may be associated with cervical dilation in inevitable or incomplete cases. Laboratory tests show a reduction in serum beta-hCG levels, which do not show the pattern of increase expected for a normal pregnancy. Transvaginal ultrasound (TV-USG) confirms the diagnosis by identifying the absence of an embryonic heartbeat or an abnormal gestational sac (Quenby et al., 2022; NICE, 2021).

The hemorrhagic syndromes of the first half of pregnancy, miscarriage, ectopic pregnancy and hydatidiform mole, have different etiologies, incidences and risk factors that contribute significantly to maternal morbidity and mortality. This survey presents the main epidemiological aspects and risk factors associated with these conditions.

Miscarriage is the most common complication of pregnancy, occurring in around 10-20% of clinically recognized pregnancies. It is estimated that the real incidence is higher, considering pregnancies that end before they are clinically detected. The miscarriage rate increases with maternal age, especially after the age of 35, reaching up to 50% in women over 40 (Cunningham et al., 2018).

Risk factors indicate that Genetic Anomalies cause approximately 50-60% of miscarriages, with trisomies, monosomy X and polyploidies being the most common (Grimes, 2016).

Other factors such as advanced maternal age, as egg quality decreases with age, increasing the risk of aneuploidies; chronic diseases such as diabetes mellitus, hypertension, systemic lupus erythematosus and antiphospholipid syndrome are associated with higher miscarriage rates (ACOG, 2021).

Infectious factors such as maternal infections like rubella, cytomegalovirus and toxoplasmosis can lead to pregnancy losses; lifestyle: smoking, excessive alcohol consumption and obesity increase the risk of miscarriage; cervical insufficiency: in

subsequent pregnancies, a history of cervical insufficiency is a significant risk factor (Cunningham et al., 2018).

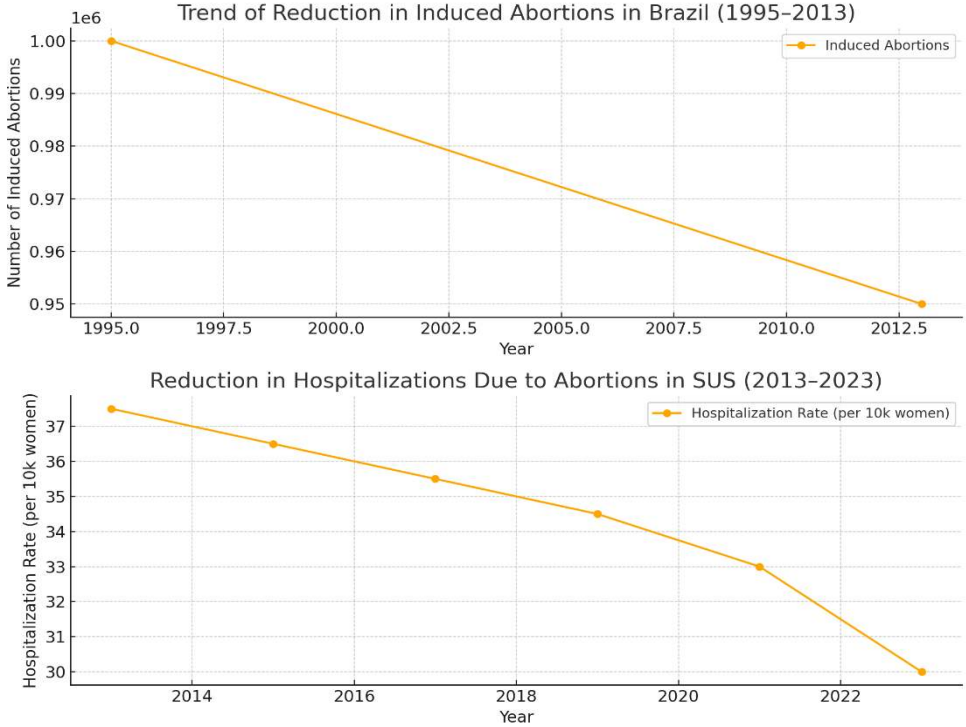
Hemorrhagic syndromes in the first half of pregnancy include conditions such as miscarriage, ectopic pregnancy and gestational trophoblastic disease (GTD). These conditions, responsible for significant maternal morbidity and mortality, require early differential diagnosis, based on clinical signs and laboratory findings, to guide clinical management (ACOG, 2021; Cunningham et al., 2022).

Brazil is a country that has stood out positively in reducing hospitalizations for abortion in recent years.

GRAPH 1 illustrates the downward trend in the incidence of abortions and related hospitalizations in Brazil: Induced Abortions (1995-2013): The number of abortions fell from approximately 1 million in 1995 to 860,000 in 2013, indicating a 26% reduction. Hospitalizations for Abortion in the SUS (2013-2023): The average annual rate of hospitalizations for abortion decreased from 37.4 to progressively lower values, with an average variation of 0.76 percentage points per year (DATA-SUS, 2013).

These trends suggest a significant reduction in abortions and associated complications in the country over the years.

GRAPH 1. Reduction in Hospitalizations for Abortion in the SUS (1995 2013/ 2013- 2023).



Source: Data SUS (1995-2013).

Another less common cause of abortion is ectopic pregnancy. Ectopic pregnancy occurs in approximately 1-2% of pregnancies and is responsible for 6-13% of pregnancy-related maternal deaths in developed countries. In low-income countries, mortality is even higher due to late diagnosis and lack of access to adequate medical care (Practice Bulletin, 2018).

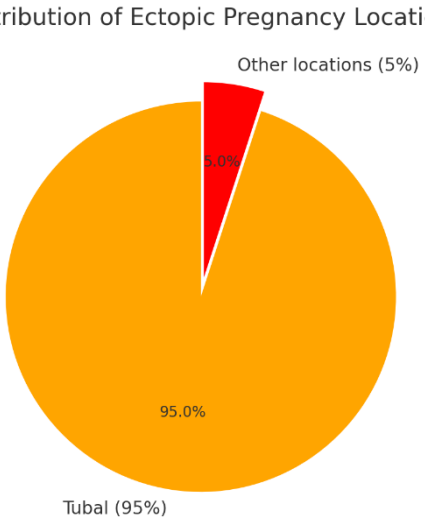
Ectopic pregnancy is characterized by the implantation of the embryo outside the uterine cavity, usually in the fallopian tubes. Clinically, it presents with severe abdominal pain, usually unilateral, and scant vaginal bleeding. Signs of hypovolemic shock may appear in cases of rupture. Laboratorially, serum beta-hCG levels are lower than expected and do not double every 48 hours, as would be typical in a normal pregnancy. The TV-USG reveals the absence of an intrauterine gestational sac and may identify an adnexal mass and free fluid in the abdominal cavity, suggestive of rupture (Barnhart, 2021; ASRM, 2022).

The risk factors identified in the literature as causes of ectopic pregnancy are; Pelvic Inflammatory Disease (PID): The main cause of tubal damage, associated with a higher incidence of ectopic implantation; Previous pelvic surgeries: Procedures such as tubal ligation and adhesion repair increase the risk of anatomical damage to the fallopian tubes; Endometriosis: Inflammation and fibrosis associated with endometriosis can compromise tubal function; Use of Intrauterine Devices (IUDs): Although the IUD reduces the overall likelihood of pregnancy, when pregnancy does occur, the risk of ectopic implantation is higher; History of Ectopic Pregnancy: The risk of recurrence in future pregnancies is significantly high; Advanced Maternal Age: Women over the age of 35 have a higher risk of ectopic pregnancy, possibly due to tubal functional alterations (Cunningham et al. , 2018).

According to the World Health Organization (WHO, 2021), we can observe how ectopic pregnancy occurs in various aspects.

GRAPH2 illustrates the location of ectopic pregnancies. It shows that 95% of ectopic pregnancies occur in the fallopian tube, with only 5% in other locations.

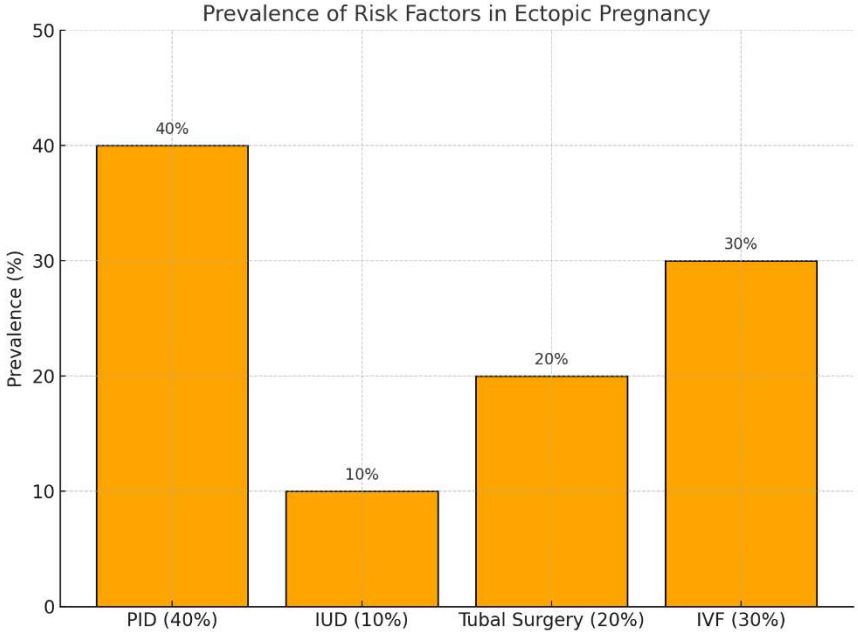
GRAPH 2. Distribution of Location of Ectopic Pregnancy.



Source: (WHO, 2021).

GRAPH 3 shows the contribution of the main risk factors, such as Pelvic Inflammatory Disease (40%) and IVF (30%).

GRAPH 3. Prevalence of risk factors for ectopic pregnancy.

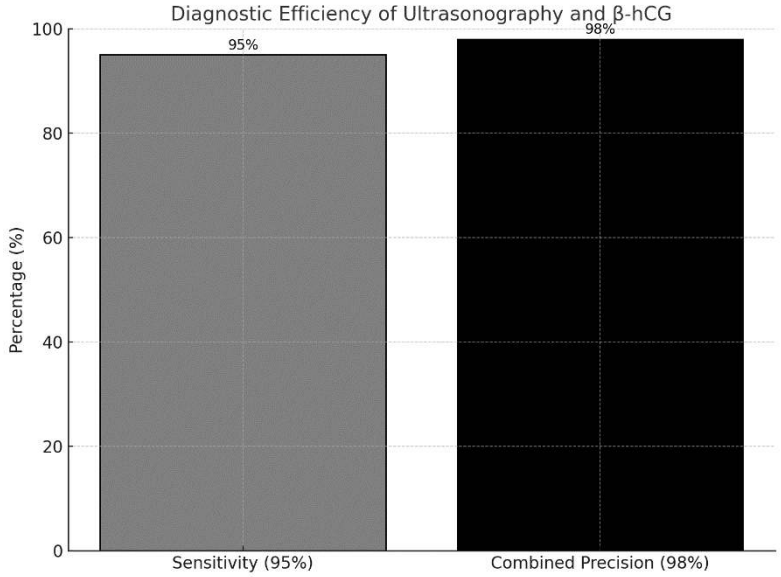


Source: (WHO, 2021).

GRAPHS 4 and 5 shows the diagnostic efficiency and success rates of treatments and complications. Diagnostic Efficiency shows the high sensitivity (95%) of transvaginal ultrasound and the combined accuracy (98%) with β-Hcg and the Success Rates of

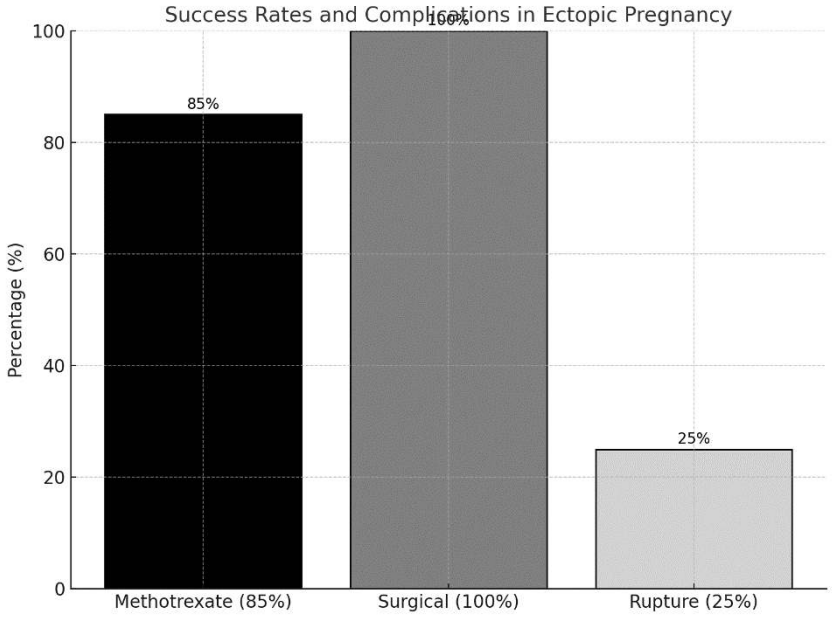
Treatments and Complications: Compares the success rates of methotrexate (85%) and surgery (100%), as well as the incidence of rupture (25%) in late diagnoses.

GRAPH 4. Diagnostic efficiency shows the high sensitivity (95%) of transvaginal ultrasound and accuracy combined with β-Hcg.



Source: (WHO, 2021).

GRAPH 5: Treatment Success Rates and Complications: Compares the success rates of methotrexate and surgery (100%), as well as the incidence of rupture in late diagnoses.



Source: (WHO, 2021).

Hydatidiform mole, a form of gestational trophoblastic disease (GTD), has a variable incidence globally. In developed countries, the incidence is around 1 in 1,000

pregnancies, while in developing countries its is as high as 1 in 100 pregnancies due to nutritional factors and genetic differences (Berkowitz & Goldstein, 2020).

GTD, which includes hydatidiform mole and choriocarcinoma, is a rare condition characterized by abnormal trophoblast proliferation. Clinical signs include persistent vaginal bleeding, often associated with the elimination of vesicles with a “grape cluster” appearance, a uterus larger than expected for gestational age and marked hyperemesis gravidarum. In the laboratory, beta-hCG levels are markedly elevated, usually well above the expected values for gestational age. On TV-USG, complete hydatidiform mole shows a “blizzard” pattern, while partial mole may show associated fetal tissue (Seckl et al., 2021; FIGO, 2021).

The differential diagnosis of hemorrhagic syndromes in the first half of pregnancy is based on an integrated assessment of clinical signs, serum beta-hCG levels and ultrasound findings. This approach allows for early intervention, reducing complications and preserving maternal health.

RISK FACTORS

- ✓ Extreme Maternal Age: Women under the age of 20 or over the age of 35 are at greater risk of developing hydatidiform mole. The risk is particularly high in women over 45, being up to 5-10 times higher (Grimes, 2016).
- ✓ History of previous hydatidiform mole: Women who have had hydatidiform mole have a 10-20 times higher risk of recurrence in subsequent pregnancies.
- ✓ Nutritional Factors: Deficiencies of vitamin A and folic acid have been associated with a higher incidence, especially in low-income countries.
- ✓ History of repeated miscarriages: Women with a history of miscarriages are more likely to develop hydatidiform mole (Berkowitz & Goldstein, 2020).
- ✓ Ethnic and Regional Factors: The incidence is higher in Asian populations, suggesting possible genetic predispositions.

Hemorrhagic syndromes in the first half of pregnancy have distinct etiologies and risk factors, but share significant impacts on maternal health. Understanding the epidemiology of these conditions and their risk factors is essential for effective interventions and reducing the associated morbidity and mortality. Public health policies should focus on prevention strategies and universal access to early diagnosis and appropriate treatment.

During pregnancy, the use of effective diagnostic tools is fundamental for monitoring maternal and fetal health, allowing for the early detection of possible complications. These tools include laboratory and imaging tests, each with specific indications throughout the different gestational stages.

Laboratory tests are essential in prenatal care, providing information on the state of health of the pregnant woman and the fetus. The main tests include:

- ✓ Complete Blood Count: Evaluates the presence of anemia, infections and other hematological alterations. Gestational anemia, for example, can be identified and treated early, preventing maternal and fetal complications.
- ✓ Blood Typing and Rh Factor: Identifies blood incompatibilities that can lead to fetal erythroblastosis. Rh-negative pregnant women with Rh-positive partners should be monitored and, if necessary, treated with anti-D immunoglobulin to prevent sensitization
- ✓ Fasting Blood Glucose and Oral Glucose Tolerance Test (OGTT): These detect gestational diabetes, a condition that can affect fetal development and increase obstetric risks. Early diagnosis allows for nutritional and, if necessary, pharmacological interventions.
- ✓ Serologies for Infections: These include tests for HIV, syphilis, hepatitis B and C, toxoplasmosis, rubella and cytomegalovirus. Detecting infections allows for appropriate treatment and preventive measures to avoid vertical transmission.

Imaging tests complement the laboratory evaluation, providing direct visualization of fetal development and maternal anatomy. The main tests include:

- ✓ Obstetric ultrasound: This is the most widely used imaging test during pregnancy, allowing fetal development to be assessed, malformations to be detected, gestational age to be estimated and growth to be monitored. Morphological ultrasound, performed between the 20th and 24th week, is essential for identifying structural anomalies.
- ✓ Dopplervelocimetry: Evaluates blood flow in the uterine, umbilical and fetal cerebral arteries, helping to detect placental insufficiency and intrauterine growth restriction. It is especially indicated in high-risk pregnancies
- ✓ Magnetic Resonance Imaging (MRI): Used in specific cases for detailed assessment of fetal anomalies or maternal conditions that cannot be

adequately investigated by ultrasound. MRI is safe during pregnancy, as long as it is performed with precise indications.

The integration of laboratory and imaging tests in prenatal care is essential for the early detection of complications and the planning of appropriate interventions. The choice of diagnostic tools must be individualized, taking into account the characteristics of each pregnancy and the risk factors present.

The management of complications during pregnancy requires well-established therapeutic approaches, which include conservative methods, pharmacological and surgical interventions. The choice of approach depends on the clinical condition, maternal stability and the desire to preserve fertility, and it is essential to integrate clinical and technological aspects for favorable results (Cunningham et al., 2022; ACOG, 2021).

Conservative or expectant management is indicated in situations where there is a prospect of spontaneous resolution or clinical stability of the pregnant woman. This method is used in: Incomplete or threatened miscarriage: When there are no signs of infection or significant bleeding, clinical surveillance associated with beta-hCG monitoring can avoid unnecessary interventions (Quenby et al., 2022); Small, stable ectopic pregnancy: Close monitoring of beta-hCG levels can be an alternative to invasive treatment, especially in low-risk pregnancies (Barnhart, 2021).

Despite its less invasive nature, this approach requires intensive monitoring to avoid complications.

Pharmacological therapy plays an important role in the management of various obstetric conditions: Abortion: The use of misoprostol for the expulsion of uterine contents is an alternative to surgical management, especially in incomplete or retained abortions. Efficacy is high, and side effects include pain and bleeding controlled in a supervised environment (NICE, 2021).

Methotrexate, a folic acid antagonist, is used in cases of non-routine ectopic pregnancy with controlled beta-hCG levels (<5,000 mUI/mL). This approach reduces the need for surgery, but requires continuous laboratory monitoring to confirm resolution (ACOG, 2021).

Chemotherapy with agents such as methotrexate or actinomycin D is indicated in cases of invasive mola or choriocarcinoma. The choice of protocol depends on the risk classification based on the FIGO score (Seckl et al., 2021).

Surgical interventions are reserved for emergency cases or failure of conservative and pharmacological approaches.

Uterine curettage or manual vacuum aspiration is indicated in abortions complicated by infection or heavy bleeding. The technique is safe, with low complication rates when performed by trained professionals (Cunningham et al., 2022).

Laparoscopy is the gold standard for the management of ruptured or critically located ectopic pregnancies. Procedures such as salpingectomy (removal of the fallopian tube) or salpingostomy (preservation of the fallopian tube) are chosen based on the patient's reproductive wishes and the extent of the damage (Barnhart, 2021).

In cases resistant to chemotherapy or in patients who do not wish to preserve fertility, hysterectomy is an effective therapeutic option (Seckl et al., 2021).

FINAL CONSIDERATIONS

The choice of therapeutic method depends on factors such as hemodynamic stability, gestational stage, the presence of comorbidities and the patient's reproductive wishes. Individualized protocols, combined with multidisciplinary monitoring, are essential to ensure safe and effective management.

Contemporary therapeutic approaches to gestational complications include conservative, pharmacological and surgical methods. The choice of the most appropriate strategy should be based on the clinical condition and individual goals of each patient, ensuring effective and safe interventions.

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