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Understanding Second Trimester Miscarriages: A Comprehensive Review

ABSTRACT

Spontaneous miscarriage is the most common complication of pregnancy. Pregnancy loss is usually multifactorial and dependent on a wide variety of genetic and epigenetic risk factors affecting either the parents or the foetus including parental age, health status, lifestyle, chromosomal abnormalities and anatomical/physiological conditions. Foetal loss during the second trimester can present with a broad range of symptoms and can be more complicated than first trimester losses due to the increased risk of haemorrhage or infection. Management of second trimester miscarriage can be divided into expectant, medical, and/or surgical interventions alongside psychological support.

Key Words: Second trimester miscarriage, Chromosomal abnormalities, Thrombophilia, Foetal loss, Uterine malformations.

INTRODUCTION

Spontaneous miscarriage is the commonest pregnancy complication, occurring in about one-fifth of clinical pregnancies. A miscarriage is defined as a spontaneous foetal loss from the time of conception until 24 weeks of gestation. The majority of miscarriages occur during the first 12 weeks of pregnancy and therefore experiencing a miscarriage during the second trimester of pregnancy is quite rare and usually takes expectant parents by surprise. A miscarriage in the second trimester is defined as a pregnancy loss after the 12th week and before the 24th week of gestation.

PRESENTATION

The most common symptoms associated with sudden pregnancy loss include uncomplicated bleeding, pain, cramping or labour. While uncomplicated bleeding is the most common presentation of miscarriage, it is important to note that not all those who experience bleeding during gestation will experience pregnancy loss. After the first trimester, a miscarriage may present with more complications including haemorrhage and infection leading to haemodynamic instability. Other symptoms of pregnancy loss may be more subclinical and subjective to each respective patient such as nausea, vomiting and decreased breast tenderness amongst others.

RISK FACTORS

A second trimester miscarriage is a clinical challenge as there are multiple potential risk factors contributing to such an event.

Epidemiological Factors

Maternal age and the number of previous miscarriages are two important independent risk factors which increase the chances of a further miscarriage event. An older maternal age has a negative impact on the amount and quality of viable oocytes. Studies have also shown that advanced paternal age also contributes to a higher miscarriage risk. The highest risk was seen among couples where the female was ≥35 years old and the male ≥40 years old.[1] Moreover, the risk of miscarriage increases with the number of previous pregnancy losses, whereby a female with a history of three consecutive miscarriages has a 40% chance of foetal loss in her next pregnancy.[2]

Other environmental risk factors which are known to negatively impact a pregnancy and therefore increase the chances of a miscarriage at any gestational age include cigarette smoking, alcohol consumption and obesity.

Genetic Factors

Parental and embryological chromosomal abnormalities can also contribute to second trimester pregnancy losses. The risk of miscarriage from chromosomal abnormalities of the embryo also increases with advanced parental age. Around 24% of second trimester pregnancy losses are due to chromosomal anomalies,

most commonly trisomy 13, 16 (almost always fatal in utero), 18, 21 and monosomy X (Turner's syndrome).

Anatomical Factors

Females with uterine malformations have been noted to have higher rates of second trimester miscarriages. Studies have shown that women born with a septate uterus are more likely to miscarry in the first trimester while those with an arcuate uterus are more prone to experience a second trimester miscarriage. In fact, retrospective research concerning reproductive outcomes has demonstrated that females with untreated uterine abnormalities have a higher risk of preterm delivery and miscarriage, whereby only half experience a full-term delivery.[3] Studies have shown that surgical correction of uterine anomalies such as hysteroscopic removal of an intra-uterine septum was associated with a reduced probability of spontaneous abortion.[3,4]

Cervical incompetence is another important cause of second trimester miscarriage. The diagnosis of cervical insufficiency is usually based on a history of pregnancy loss preceded by painless cervical dilatation and spontaneous rupture of membranes. Factors which may contribute to a higher incidence of cervical incompetence include previous cervical trauma such as cone biopsy, high parity, and prior foetal losses during the second trimester.

Infective Agents

Infection has been shown to account to 10-25% of second trimester miscarriages, especially in developing countries due to a multitude of factors including higher rates of vector-borne infections such as syphilis and malaria as well as region-dependant barriers to appropriate healthcare.[5,6] The presence of bacterial vaginosis during the first three months of pregnancy is an independent risk factor for second trimester miscarriage and preterm delivery. A randomised controlled trial has outlined the importance of treating bacterial vaginosis early on with clindamycin in order to reduce the incidence of a second trimester miscarriage or preterm labour.[7]

Thrombophilia

A retrospective meta-analysis on the impact of inherited and acquired thrombophilia disorders in miscarriages showed that a non-recurrent pregnancy loss between 20 to 24 weeks gestation is strongly associated with factor V Leiden, protein S deficiency and the prothrombin gene mutation.[8] Thrombophilias have been considered as a cause for recurrent miscarriages and late pregnancy complications, namely due to thrombosis of the uteroplacental circulation.

The presence of anti-apolipoprotein H antibodies, specifically anticardiolipin and lupus anticoagulant in females with systemic lupus erythematosus, antiphospholipid syndrome or other immunologic disorders are a principal risk factor contributing to second and third trimester miscarriages. Such antibodies give rise to placental thrombosis and thus all females with a history of one or more second trimester foetal loss should be screened for possible hypercoagulable state disorders.

MANAGEMENT

The management of second trimester miscarriages depends on the clinical presentation of the woman and the underlying cause of the pregnancy loss. In cases where the miscarriage is inevitable, expectant, medical or surgical management can be offered to the patient.

Expectant management is reserved for clinically stable patients in whom the miscarriage is allowed to occur naturally without any medical intervention.

Medical management involves the use of medications such as misoprostol to induce uterine contractions and expel the products of conception. This method is usually preferred in cases where the woman is stable and has no signs of infection. The success rate of medical management varies however, it is generally very high and can be associated with minimal discomfort and side-effects.

Evacuation of the retained products of conception (ERPC) is a procedure usually performed under general anaesthesia for the surgical management of a miscarriage after diagnosis is confirmed. The success rate of surgical management is also high, however, it carries a higher risk of complications such as bleeding, infection and uterine perforation.

Psychological Support

The loss of a pregnancy can be a traumatic experience for the couple. It is important that healthcare professionals provide adequate psychological support to all parties involved during this difficult time. Counselling and support groups can help such patients cope with the emotional distress associated with the loss of a pregnancy.[9]

PREVENTION OF SECOND TRIMESTER MISCARRIAGES

While some risk factors for second trimester miscarriages are not reversible, there are some risk reducing interventions to prevent second trimester miscarriages. These include:

1. Maintaining a healthy lifestyle: Eating a healthy diet, engaging in regular physical activity, avoiding

cigarette smoking and excessive alcohol consumption can help reduce the risk of pregnancy loss.
2. Monitoring chronic medical conditions: Women with chronic medical conditions such as diabetes, thyroid disorders, and PCOS should work closely with their healthcare provider to manage their condition during pregnancy.
3. Genetic counselling: Couples with a history of chromosomal abnormalities should consider genetic counselling to assess their risk of future pregnancy losses and discuss options such as pre-implantation genetic testing.
4. Early detection and treatment of uterine anomalies: Women with a history of second trimester miscarriages should undergo a thorough evaluation to assess for uterine anomalies. If an anomaly is detected, early surgical intervention may be recommended in certain cases.
5. Follow up screening: Women with a history of second trimester miscarriage should be screened before the next pregnancy for antiphospholipid antibodies and thrombophilias.

CONCLUSION

A miscarriage is the most devastating outcome of a pregnancy, and while the majority of cases occur in the first trimester, the intent of this article is to highlight the importance of second trimester miscarriages as an important prognostic factor for the outcome of future pregnancies. A variety of risk factors, both genetic and epigenetic, can result in spontaneous foetal loss, most of which are difficult to pre-emptively diagnose or test for prior to conception. Other risk factors are more modifiable such as the testing for congenital uterine malformations, screening for transmissible diseases and taking into account maternal age when attempting to conceive.

Independent to the pathophysiological process of miscarriage, treatment remains largely congruent and divided into medical (hormone-assisted delivery of the foetus), surgical (removal of retained products of conception) or simply via supportive expectant management. The management and investigation into the cause of abruption of pregnancy requires a multidisciplinary approach taking primarily into careful consideration the physical and mental wellbeing of the patient.

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