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Recurrent miscarriage and factors that effects its: A review

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ABSTRACT: Spontaneous abortion is a commonly occurring issue during human pregnancy. The definition provided by the WHO in 1977 is universally accepted. Recurrent pregnancy loss is a multifaceted health issue that lacks a universally agreed-upon definition. The lack of agreement in definitions encompasses not only the varying number of spontaneous abortions (two or three) that are considered recurrent pregnancy losses but also the different types of pregnancies and the gestational age at which the miscarriage occurs. The prevalence among clinical pregnancies is approximately less 15%, but when early pregnancy losses are included, it rises to 17–22%. The only two etiologic causes that all authors agree on are uterine abnormalities and paternal balanced chromosomal rearrangements. Numerous alternative risk variables have been proposed.

Keywords: Spontaneous abortion, Recurrent pregnancy, miscarriage, factors

1. INTRODUCTION

Miscarriage may be regarded as among the many prevalent complications that might develop during pregnancy in persons. Numerous definitions have been put up for this medical condition, but the most widely acknowledged one is the one introduced by the World Health Organization (WHO) in 1977. Subsequently, Miscarriage is the medical term used to describe the expulsion or removal of a developing child or embryo weighing five hundred grams or less from the placenta of its wife [1].

The prevalence of miscarriage, as shown by multiple authors in clinical pregnancies, is approximately 12–15%. The numerical value should be augmented when considering early pregnancy losses, which are characterized as pregnancy terminations that transpire roughly 14 days after conception, coinciding with the subsequent menstrual cycle, and can be mistaken for regular menstrual flow. The documented prevalence of these early pregnancy losses is approximately 17–22% [2]. A miscarriage, also known as spontaneous abortion, refers to the termination of a pregnancy before the completion of twenty-three weeks gestation. Vaginal bleeding is a prominent indicator of a miscarriage. Recurrent pregnancy loss is the term used to describe the loss of three consecutive pregnancies, including undetectable ones. Miscarriage, sometimes known as "spontaneous abortion," is a common complication during pregnancy, and as of right now, there are no biomarkers that can be used to predict the likelihood of the occurrence in asymptomatic patients. When the leftover intrauterine products of conception are not regularly evacuated, a missed abortion (MA), a form of miscarriage, can end in embryonic or fetal mortality. Despite the lack of obvious symptoms, 8–20% of clinically confirmed pregnancies have miscarriage [3].

When compared to a group of women who had abortions, the serum level of vitamin D3 in healthy pregnant women was higher. When comparing the serum zinc levels of aborted women to those of healthy pregnant women, a downward trend was seen [4].

Serum Superoxide dismutase (SOD) and Malondialdehyde (MDA) levels in aborted women showed markedly different levels from those in the healthy pregnant group. There was a decrease in the mean serum SOD level in aborted women compared to healthy pregnant women, and the MDA level was higher in the aborted group than in the healthy delivered women [5].

Zinc (Zn) is an essential trace element for immune function and plays a major role in the immune response against infections. Essential vitamins and minerals, such as zinc metal and vitamin D, support maternal health and fetal

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development through mechanisms that are integrated across placental, maternal, and fetal compartments. However, deficiencies or excesses in these trace elements are typically linked to human diseases. Zinc is present in all living organisms and tissues. The body's defenses against infections are influenced by the serum amount of vitamin D, which also controls how well the immune system performs [6].

2. Placental structure and function

Substances must be transferred via the fetal capillary bed, cytotrophoblast, syncytiotrophoblast, and villous basement membrane. After conception, the fertilized oocyte passes through the fallopian tube to establish itself in the uterine cavity [7]. As the pregnancy progresses, the fertilized oocyte goes through the ensuing developmental phases. The differentiation process between the blastocyst and the morula stage of development is initiated by a specialized cell line called the trophoblast. The fluid that builds up inside the morula and forms the blastocyst cavity is released by the cells called blastomers, which make up the morula, about 4 days after conception [8]. At this stage, an outer mononuclear layer of cells forms the trophoblast, which encloses the blastocyst cavity, and an inner compact cell mass forms the embryoblast. About 6-7 days after conception, the blastocyst attaches itself to the uterine decidua, at which point the placenta starts to grow. Rapid division and fusion between the cytotrophoblast and syncytiotrophoblast occurs. As a result, the cytotrophoblast allows the syncytiotrophoblast to grow. The placental membrane, which is made up of the following layers, divides the blood of the mother and the fetus from one another [9].

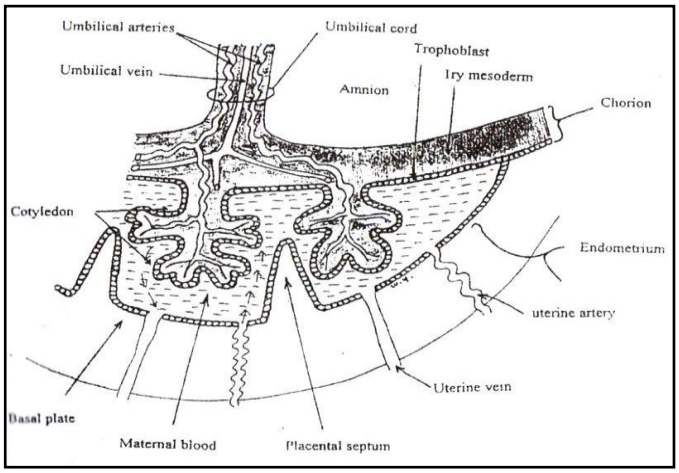

FIGURE 1. - Diagram showing the maternal and fetal blood circulation in the placenta

There are two umbilical arteries and one sizable umbilical vein in the umbilical cord. These blood vessels carry oxygen and carbon dioxide to and from the placental tissues, where the exchange between the mother and the fetus occurs. During its life, it performs functions that are similar to those of the pituitary gland (synthesis of gonadotropic and prolactin-like hormones), pituitary and gonads, lung (gas exchange), intestine (nutrient absorption), kidney (excretion and ion regulation), liver (synthesis of serum proteins, steroid metabolism), kidney (incomplete synthesis of progestins, estrogens), and gut (nutrient absorption) [10].

3. Factors Effect in Abortion

3.1 Vitamin D and Miscarriage

Vitamin D deficiency (low serum levels of 25-hydroxyvitamin D (25(OH)D)) is a serious health concern, especially among pregnant women and those who are hoping to become pregnant. Women who experience serious obstetric and reproductive issues, such as preeclampsia, gestational diabetes, and premature birth, are more likely to suffer from vitamin D deficiency [11]. This is because vitamin D deficiency is frequently has closely association with bone problems in both pregnant women and babies. deficiency in vitamin D is a common concern among women in developed countries who are fertile, and it may be increasing. There are probably many contributing factors, but inadequate sun exposure and vitamin D consumption are two of them. Women who avoid the sun, especially those who reside in colder climates, and vegetarians [4, 12].

3.2 Calcium and Miscarriage

Pregnant women who have severe nutritional deficiencies or hypoparathyroidism may experience hypocalcaemia, though this is rare. It has been related to hypertensive diseases, has been demonstrated to increase the risk of preeclampsia and problems with fontal development, and can result in a number of pregnancy-related complications for both the mother and the fetus. There is a link between hypocalcemia and high blood pressure, according to recent studies. Research conducted on sheep has shown that fasting during the latter stages of pregnancy might lead to maternal low calcium levels, resulting in increased blood pressure and decreased uterine blood flow. The risk of developing hypertension during pregnancy is inversely correlated with calcium consumption [13].

3.3 Zinc and Miscarriage

Pregnant women who are zinc deficient are at risk for dangerous and irreversible outcomes such as congenital malformations, intrauterine growth retardation (IUGR), vulnerable growth impairment, spontaneous abortion, low birth weight (LBW), preeclampsia, delayed immune system development, premature neurobehavioral development, and an increased mortality rate [14].

Zinc is a vital trace element that the body uses for a number of purposes. The body goes through various processes, such as cell division, muscle growth, hormone function, blood coagulation, hair and nail growth, immune system function, abnormalities in women's menstruation, regeneration, reproduction, and male fertility. The immune system and zinc have a complex relationship. Immune responses may become less effective if zinc levels are low because zinc has a significant impact on both specific and nonspecific immune responses.

3.4 Caffeine

Caffeine is a stimulant compound that is commonly found in drinks such as coffee, tea, and energy drinks. Caffeine is a common compound found in many commonly used drugs. The primary source of this substance is coffee, with an average content of 107 mg per cup. The gastrointestinal tract absorbs caffeine easily, and it travels throughout all of the body's tissues [15]. Furthermore, it traverses the placenta. However, for a pregnant woman, the duration is extended to 10.5 hours. The duration of the newborn's sleep is typically between 32 and 140 hours. Consuming tobacco leads to a decrease in the time it takes for caffeine to be eliminated from the bloodstream, resulting in a 200% increase in caffeine levels when smoking is ceased [16].

3.5 Tobacco

Multiple investigations have established a correlation between spontaneous abortion and tobacco use. However, previous research has reported these findings in other studies. Many constituents of tobacco have been identified as potential poisons that may explain the association with abortion. Nicotine is the most crucial component. Vascular spasms can lead to vasculitis, which in turn can cause placental disease. However, there is currently no evidence to support its existence or the specific way in which this drug works. There is little empirical data to substantiate the claim that tobacco usage escalates the likelihood of trisomy [17].

3.6 Alcohol

Alcoholism is widely recognized to have numerous detrimental impacts on the development of a fetus. It has the ability to generate the fetal alcohol syndrome. There is no recommended amount of alcohol that is considered safe to consume during pregnancy [18].

Its correlation with miscarriage is relatively obscure. The occurrence of elevated abortion rates in women with alcoholism has been reported, however, it remains unclear if this is directly caused by alcohol consumption or if it is a result of secondary complications associated with alcoholism, such as cirrhosis. Furthermore, alcohol blood levels exceeding 200 mg/dl have the potential to directly induce spontaneous miscarriage [1].

However, the connection between moderate alcohol use and spontaneous abortion remains uncertain. Multiple investigations, such as the one conducted, provide evidence confirming this correlation. The study indicates that the danger is only present in women who regularly use a moderate amount of alcohol (one or more drinks), but not in those who consume alcohol seldom.

3.7 Maternal age

Multiple studies have shown a correlation between advancing maternal age and an elevated likelihood of experiencing a miscarriage. The data estimation suggests that a patient aged 30-32 had a relative risk of miscarriage of 2.1% (with a 95% confidence range ranging from 1.0% to 4.0%). The incidence rate ratio in patients aged 33 or older is 2.8% (95% confidence interval 1.5–5.9%). However, the risk of complications significantly increases in patients over the age of 35. In individuals over the age of 40, the risk is five times greater compared to those between the ages of 31 and 35, resulting in a risk range of 20–40% [19].

The relationship between the age of the donor and the abortion and pregnancy rate in IVF programs with donated oocytes has been proven to be significant. This means that the age of the donor is the most crucial factor in predicting the outcome of the IVF program in terms of abortion and pregnancy rates. Furthermore, the occurrence of chromosomal abnormalities increases as one ages [20].

3.8 Cytokines

The formation of miscarriage has been linked to the endometrial expression of certain chemicals known as cytokines, as well as the activation of specific cells. Therefore, an increased concentration of gamma interferon or tumor necrosis factor-related factor (TNF), or enhanced stimulation of natural killer cells, may contribute to an increased likelihood of miscarriage. Conversely, an elevated level of interleukin-10 may be linked to a reduced risk [21].

3.9 Sexual activity

Several studies have suggested that sexual intercourse during early pregnancy may lead to uterine cramps, hence raising the risk of miscarriage [22].

3.10 Maternal injuries

Spontaneous abortions are often attributed to maternal trauma. However, the investigations conducted in this manner were unable to definitively establish a direct link between trauma and the occurrence of a miscarriage. A correlation between the injured skin area and severe maternal burns has been documented [23].

3.11 Interpregnancy interval

A study conducted on the Laestadius religious cult, who adhere to a strict no contraception policy, found no significant variation in the rate of miscarriages based on the duration of time taken to achieve conception. However, a study conducted by Srisuphan and Bracken indicates an increased likelihood of miscarriage in women who conceive within 6 months following their last pregnancy [24].

4. Symptoms belong to APS

Due to blood clots, APS can result in both mild symptoms and potentially lethal events. The most frequent and possibly curable cause of recurrent miscarriages during pregnancy is APS, which is also linked to other issues like pre-eclampsia, low birth weight babies, and stillbirth [25].

More people than others are impacted by the symptoms. On the other hand, some people have blood levels of antiphospholipid antibodies (APL) but do not experience any symptoms, blood clots, or problems during pregnancy. Because there is still a great deal of research to be done, we do not yet know why these anomalies exist.

The following are typical low-grade APS symptoms, migraines and headaches, memory issues, lightheadedness and trouble balancing, cognitive (mental) challenges, joint discomfort exhaustion [26].

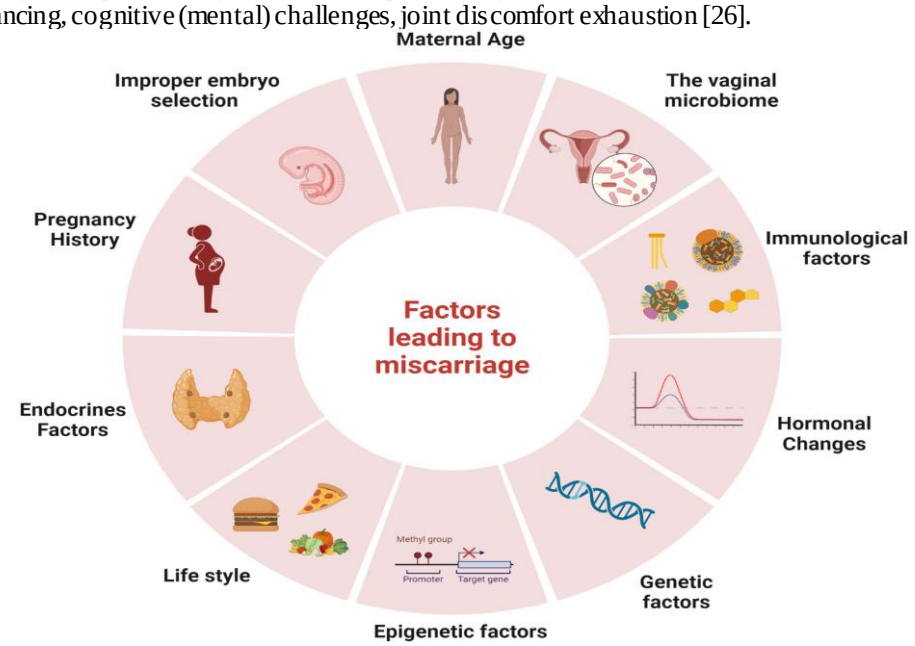

FIGURE 2. - Diagram showing the Maternal age

5. Malondialdehyde (MDA) and Miscarriages

Malondialdehyde is a dangerous compound that is produced when polyunsaturated fatty acids undergo autooxidation. It is an important indicator of oxidative damage, can interfere with several membrane functions, including the fluidity and ability of the membrane to let molecules in and out. It can also prevent the activity of enzymes. An excess of lipid peroxides, a weakened antioxidant defense system, and/or a greater concentration of lipid peroxides in the decidua and villous of women experiencing early pregnancy missing are all associated with elevated MDA levels.

Oxidative stress (OS) arises when there is an excess of ROS production, insufficient antioxidant intake, or increased ROS utilization relative to the amount of ROS and other radical species that are being scavenged by antioxidants. Oxidative stress (OS) occurs due to an elevation in the levels of free radicals, production, and/or reactive oxygen species (ROSs), coupled with a decline in the biological system's ability to efficiently eliminate the reactive intermediates or repair the resulting damage. Because OS plays a pathophysiologic role in the placental enzymes and fetus, increased free radical activity is seen in pregnant women with conditions like preeclampsia, spontaneous abortion, and intrauterine growth restriction [27].

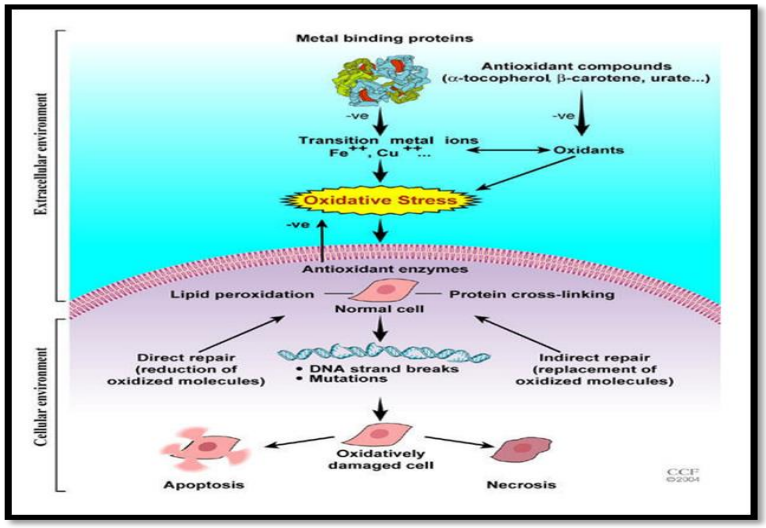

FIGURE 3. - Diagram showing Oxidative stress and metal binding protein

6. Medications affect miscarriage

Medications that include methotrexate, retinoids, misoprostol, and non-steroidal anti-inflammatory medicines increase the likelihood of miscarriage during this period. Pregnant women should get advice from their doctor, pharmacist, or midwife before starting any new medicine [28].

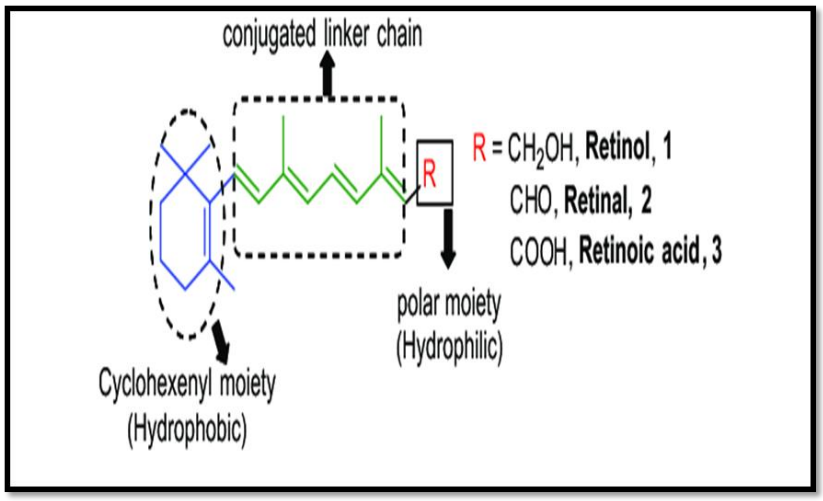

FIGURE 4. - Chemical Structures of some drugs

7. Medications that prevent miscarriage

It has been suggested that some women who miscarry may not make enough progesterone in the early part of pregnancy. Supplementing these women with medications that act like progesterone (these are called progestogens) has been suggested as a possible way to prevent recurrent miscarriage [29, 30].

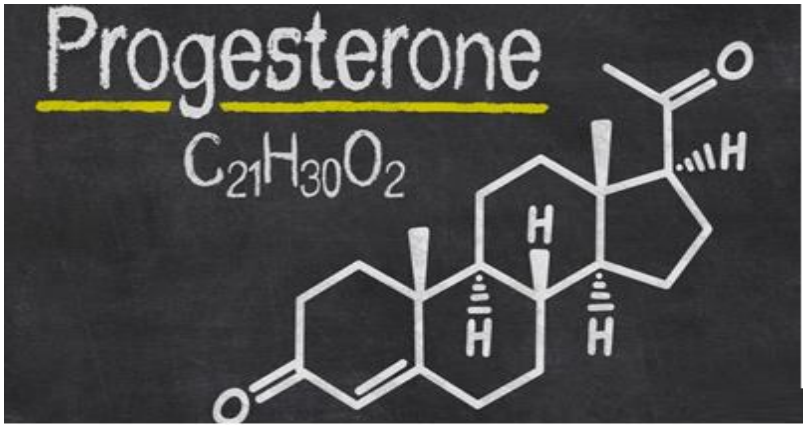

FIGURE 5. - Structure of progesterone

8. CONCLUSION

Recurrent miscarriage is a distressing occurrence that has a significant impact on the physical and psychological well-being, as well as the social welfare, of women. Various international protocols for managing recurrent miscarriages are endorsed and incorporated into clinical practice. However, these standards adhere to varying definitions of Recurrent pregnancy, rendering the calculation of recurrent miscarriage epidemiology imprecise. Furthermore, due to the discrepancies in terminology, these guidelines provide a distinct therapeutic strategy following either two or three instances of pregnancy loss, resulting in an inconsistent overall approach to the problem.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

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