fortune Journals

Research Article

OBSTETRICS AND GYNECOLOGY RESEARCH

ISSN: 2637-4560

Management Strategies for Miscarriage: A Literature Review of Current Clinical Practices and Emerging Treatments

Zlatko Kirovakov*[,1,2], Antonio Dushepeev[1,3], Stefani Markova[1,3]

Abstract

Early miscarriage, defined as the loss of pregnancy before the 12th week, affects 10-20% of clinically recognized pregnancies. Curettage has traditionally been the standard procedure, but expectant management and medical therapies have gained prominence in recent years. This review examines current treatment strategies for miscarriage. Recurrent miscarriage (RM), defined as three or more consecutive pregnancy losses, and affects 1-2% of women. While early miscarriage is common experience, recurrent miscarriage poses unique challenges that require distinct management strategies. RM is often linked to elevated anti-phospholipid antibodies (5-15%), sperm DNA damage (up to 85%), and hyper-receptive endometrial stromal cells, which can accept low-quality embryos. Women with thyroid-related antibodies or elevated TSH levels are at a higher risk of miscarriage, with researchindicating a doubled risk in the first trimester. This review analyzes literature and guidelines published between 2018 and 2024, highlighting three primary treatment options: expectant care, medical therapy, and surgical intervention. The PRISMA method was employed for systematic review and data extraction from studies published in this period. Expectant management offers a non-invasive option with a success rate of 80-90%, while misoprostol is a medical approach with success rates between 75-90%. IVF with genetic testing is recommended for RM associated with chromosomal abnormalities, with success rates of 50-70%. Hysteroscopic metroplasty has a 60-85% success rate for women with uterine malformations, such as a septate uterus. Progesterone therapy can improve live birth rates by 20-30% in women with a history of multiple miscarriages. A combination of low-molecular-weight heparin and aspirin is more effective than aspirin alone, improving outcomes by 30-40% in women with antiphospholipid syndrome. While curettage remains the standard procedure for severe cases, expectant and medical therapies are effective alternatives, particularly when addressing underlying causes of RM. Advances in personalized care show promise for improving outcomes in affected women.

Keywords: Miscarriage, Management and Clinical Practices, Expectant Therapy, Medical Therapy, Surgical Intervention

Introduction

Miscarriage, also referred to as spontaneous abortion, is a common problem seen in pregnancy, affecting approximately 10-20% of clinically identified pregnancies. It can be caused by chromosomal abnormalities, problems with the uterus, hormonal disorders, infections, or immunological dysfunctions among others, and it refers to the loss of a fetus before the 24th week of gestation [1]. People who have suffered a miscarriage carry the heavy emotional and psychological

Affiliation:

[1]Department of Obstetrics and Gynecology, University Multiprofile Hospital for Active Treatment – Burgas, Burgas 8000, Bulgaria.

[2]Department of Health Care, Faculty of Public Health and Health Care. Burgas State University "Prof. d-r Asen Zlatarov'' – Burgas 8000, Bulgaria,

[3]Faculty of Medicine. Burgas State University "Prof. d-r Asen Zlatarov'' – Burgas 8000, Bulgaria.

***Corresponding author:**
Zlatko Kirovakov, Department of Obstetrics and Gynecology, University Multiprofile Hospital for Active Treatment – Burgas, Burgas 8000, Bulgaria

Citation: Zlatko Kirovakov, Antonio Dushepeev, Stefani Markova Management Strategies for Miscarriage: A Literature Review of Current Clinical Practices and Emerging Treatments. Obstetrics and Gynecology Research. 8 (2025): 59-71.

Received: March 24, 2025
Accepted: March 27, 2025
Published: April 05, 2025

Kirovakov Z, et al., Obstet Gynecol Res 2025
DOI:10.26502/ogr0180

burden and the physical process of healing from a miscarriage can be problematic as well [2]. Recurrent miscarriage is defined as the loss of three or more consecutive pregnancies. It is extremely distressing and often indicative of some underlying medical conditions that require more specialized care [3].Supportive measures, such as expectant management or surgical procedures like dilatation and curettage, were the mainstay of miscarriage therapy in the past. As scientific understanding of the causes of miscarriages has advanced, management strategies have also evolved, with increasingly personalized, evidence-based therapies becoming the standard of care [4]. Medical treatments, including manual vacuum suction and misoprostol, which cause uterine contractions, are frequently utilized in situations of early miscarriage [5]. Better ultrasound equipment currently makes it possible to detect embryonic abnormalities sooner, and genetic screening for couples who experience repeated miscarriages has been developed as a result of advancements in genetic research [6]. Figure 1 shows the leading factors of miscarriage.

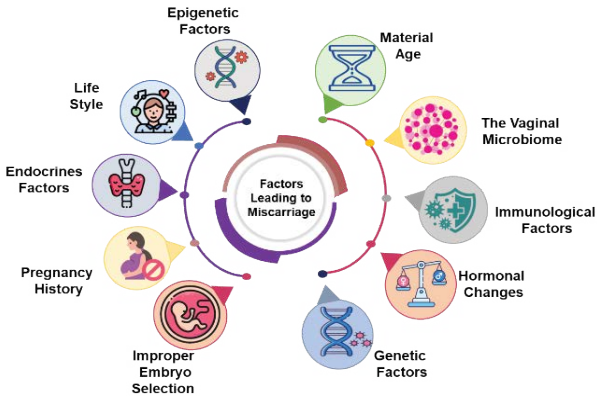

Figure 1: Factors leading to Miscarriage

Recently emerging pharmacological treatments for miscarriages include immunological treatment, and hormone replacement therapies. New treatment paradigms, such as the use of low-dose aspirin and heparin therapy in women with antiphospholipid syndrome, have been developed as a result of recent research that examined the involvement of thrombophilia, autoimmune illness, and immune-related variables in miscarriage [7]. Moreover, the use of probiotics and anti-inflammatories has been suggested as potential therapeutic interventions to improve pregnancy outcomes given the increasing focus on the microbiota, and uterine environment [8]. Despite these advancements, managing miscarriages continues to be a challenging area of care. The most significant issue is the inability to define with precision the cause of miscarriages, especially in early-stage losses; chromosomal abnormalities are the most common cause, but other factors like hormonal imbalances, immune dysfunctions, and uterine anomalies can go undiagnosed [9]. Furthermore, the lack of widely accepted diagnostic criteria for recurrent miscarriages complicates treatment decisions to be made in treatment and causes differences in clinical practices. Finally, many new treatments, especially immune therapies, haven't conclusively proven their ability to improve pregnancy outcomes based on large-scale, randomized controlled trials [10].

Methodology

Data extraction and systematic review were conducted using the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) technique, which guaranteed an organized and open process. It entailed choosing research according to predetermined standards, evaluating their caliber, and obtaining pertinent information. The goal of the procedure was to pinpoint important discoveries about the available treatments for miscarriages. The review consolidated information on success rates and possible risk factors linked with various medicines by according to the PRISMA recommendations. This approach improved the dependability of the results reached by organizing the data in a clear and consistent way. The PRISMA method was applied to ensure a rigorous systematic review, with inclusion criteria focusing on studies published within the last decade evaluate both clinical and emerging treatment options. Figure 2 depicts the PRISMA overview.

Search Process

Studies published between 2018 and 2024 from Trinka, PubMed, Google Scholar, and Web of Science served as the foundation for the search strategy used for the review. Search keywords included early miscarriage, recurrent miscarriage, expectant management, medical therapy for miscarriage, IVF with genetic testing, progesterone therapy

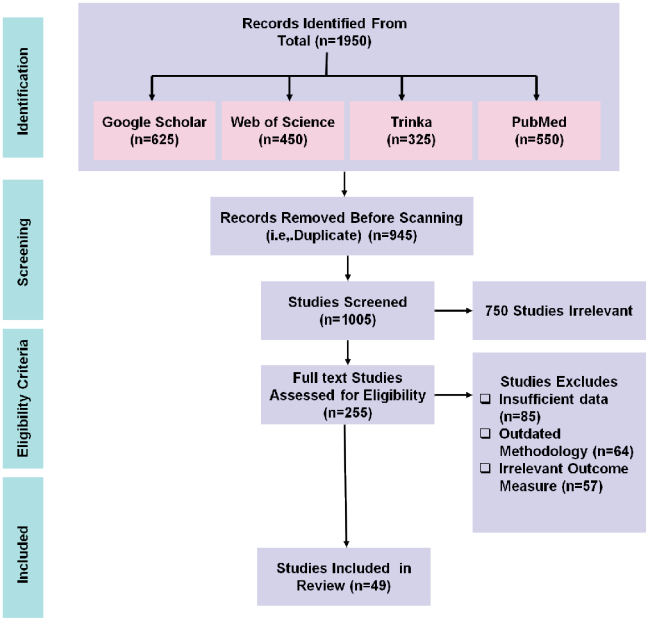

Figure 2: Overview of PRISMA structure

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for miscarriage, antiphospholipid syndrome treatment, in hysteroscopic metroplasty. Clinical trials, meta-analyses, and established recommendations were prioritized when filtering articles based on their relevance, peer-reviewed status, and publication date. To guarantee a thorough collection of pertinent material, references from important journals were also examined.

Eligibility Criteria

Recurrent miscarriages (three or more consecutive losses) or early miscarriages (before the 12th week) are criteria for eligibility in this evaluation. Participants should have a diagnosis of diseases including hyper-receptive endometrial stromal cells, thyroid-related antibodies, sperm DNA damage, or increased anti-phospholipid antibodies. People looking for therapeutic choices including medicinal therapy, surgical intervention, and expectant care are the main focus of the review. Uterine abnormalities are significant cause for repeated miscarriages.

Data Extraction

A PRISMA technique was used to gather data, gathering pertinent information from research that were published within the allotted period. Important variables were thoroughly examined, such as treatment results, success rates, and related risk factors. To make judgments on the efficacy of various therapeutic procedures, the gathered data was then combined. This procedure ensured the evaluation included the most recent and pertinent research to comprehend the treatment of early and recurrent miscarriages.

Etiology and risk factors for miscarriage

Early pregnancy difficulties are frequent and can be caused by several different reasons. To improve treatment and preventative tactics, it is crucial to comprehend the fundamental causes and risk factors. Figure 3 shows the risk factors of miscarriage.

Elevated anti-phospholipid antibodies

Pregnancy complications are significantly influenced by aPL, which is present in 5–15% of the general population. Recurrent pregnancy loss and first-trimester miscarriage are among the adverse pregnancy outcomes that are significantly associated with increased levels of aPL [11]. The risk of pregnancy problems is considerably increased for women with elevated aPL, even if they do not have a history of thrombosis. However, the risk of miscarriage remains high, particularly in women who are asymptomatic or have never experienced a thrombotic event, even though primary thromboprophylaxis is typically not advised for asymptomatic aPL-positive women. Higher aPL titers raise the chance of miscarriage, especially when LA or triple positivity (positive LA, aPL, and anti-β2GPI antibodies) are present [12]. Thromboprophylaxis with LDA and LMWH improves pregnancy outcomes associated with increased aPL. While LMWH is especially helpful in lowering thromboembolic risks during pregnancy and the postpartum period, LDA lowers the chance of miscarriage in the first trimester. According to the research [13], thromboprophylaxis is recommended for high-risk individuals, including those with a history of pregnancy complications or persistently positive aPL antibodies. For these women, LMWH and LDA offer a treatment strategy to reduce their risk of thrombosis and miscarriage.

Sperm DNA damage

A single-cell gel electrophoresis (alkaline Comet) assay, which has already been modified for human spermatozoa, was used to assess the fragmentation of sperm DNA. This technique can be used to determine the level of variability in DNA quality amongthe total sperm population in semen as it quantifies the amount of DNA damage in each spermatozoon. Before being embedded in agarose gel, aliquots of native semen were adjusted to a sperm concentration of 2×10 ml^{-1} using phosphate buffered saline. Then, fifty sperm cells

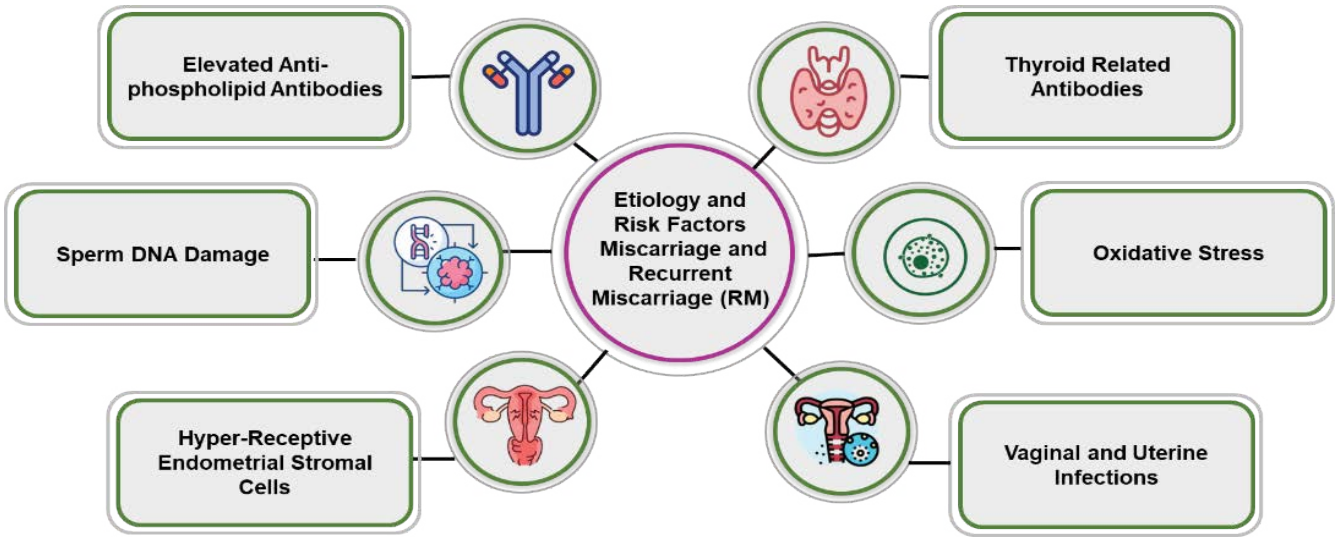

Figure 3: Etiology and Risk Factors for Miscarriage

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DOI:10.26502/ogr0180

per slide were analyzed in duplicate using membrane lysis, electrophoresis, Comet scoring, and protamine and histone elimination. Every stage was completed in a controlled setting concerning temperature and humidity to avoid causing harm to DNA while processing [14]. According to a meta-analysis, couples in whom the male partner had higher levels of sperm DNA damage were more likely to experience miscarriage than controls that suffered minimal or no sperm DNA damage. Studies indicate that up to 85% of RM cases may involve some degree of sperm DNA damage, highlighting the need for comprehensive assessment [15].

Hyper-receptive endometrial stromal cells

In humans, inadequate chromosomal segregation is a hallmark of early embryonic development and gamete production. A high frequency of embryo genetic instability is primarily responsible for the estimated 50% of human embryos that die during pregnancy, particularly before the blastocyst stage. The medical importance and potential benefits of this common mosaicism and aneuploidy in human embryos are yet unknown. However, several researchers suggest that clever maternal methods have developed to deal with genomically unstable blastocysts in a discriminatory manner, preventing unnecessary investment in invasive but incompetent embryos [16]. According to a recently developed theory, the appropriately decidualized endometrium is essential for embryo biosensing and selection, processes that could be interfered with uRM. The biosensor's operation of decidualized endometrium following implantation was demonstrated in a significant analysis. The coculture of human ESCs with an arresting human embryo markedly inhibited the release of key implantation mediators and HB-EGF. Moreover, embryonic defects elicit ER stress in human decidual cells, but developmentally normal embryos activate beneficial metabolic enzymes and implantation factors. Together with the positive and negative mechanisms, the decidual endometrium actively selects embryos during implantation.Several strong in vitro findings support the hypothesis that endometrial receptivity to the quality of the embryo could be compromised in uRM. This theory is also consistent with the clinical finding that many uRM women report abnormally high pregnancy rates. In other words, women with uRM are not rejecting normal embryos, but instead, they exhibit an increased receptivity to the implantation of embryos that are unlikely to thrive, compared to healthy women. uRM sufferers are not discarding normal embryos, but rather are more receptive or hyper-receptive to the implantation of embryos that will never survive than healthy women. In vitro, decidualization in fourteen people results in greater amounts of the pro-implantation cytokine PROK1 and reduced levels of the decidual biomarker prolactin. This results in increased uterine receptivity, but uRM is supported by attenuated embryo selection. Additionally, the ESCs produced from uRM are less able to distinguish between substantial and insufficient embryos and are more inclined to expand the trophoblast spheroids. Simultaneously, the observation of uRM women's lower TTP and greater MFR compared to the controls provides clinical support. The average human MFR, or the chance of becoming pregnant during a menstrual cycle, ranges from twenty to thirty percent, which is negligible in comparison to various mammals. With an MFR above sixty percent, forty percent of uRM women were super fertile. Moreover, although uRM women have a higher maternal age, their TTP is significantly lower than that of normal women [17].

Thyroid-Related Antibodies

Pregnancy-related subclinical hypothyroidism is linked to an elevated RM risk. Women who had positive TPO-Ab were more inclined to experience sporadic and RM. Furthermore, women with TSH levels greater than 2.5 mIU/L during the first trimester had a twofold increased risk of miscarriage. Thyroid antibodies do not impact the outcome of a subsequent pregnancy in euthyroid women with a history of RM. A high TSH level combined with a low FT4 level was considered hypothyroidism. The correlation between baseline ATA positive and the occurrence of thyroid irAEs was examined [18].

Oxidative stress (OS)

OS has been proven to play an important role in RPL, and many biomarkers are used in clinical evaluations to measure oxidative stress. Some of these biomarkers are H_2O_2, MDA, and markers of oxidative DNA damage such as 8-OHdG. In most of the research conducted, RPL patients are shown to have higher levels of oxidative stress markers like SOA and H_2O_2 compared with controls [19]. These high levels are associated with weakened antioxidant defenses, especially low activities of the key enzymes that would otherwise serve to defend cells against oxidation, including SOD and CAT. In the placenta, NADPH oxidase generates superoxide. Oxidase contributes to the oxidative environment, especially in the early stages of pregnancy; the imbalance between oxidative species and antioxidants are especially important. Lipid peroxidation, which destroys cell membranes and impairs cell activities, is a result of oxidative stress in the placenta and plasma in RPL patients. Research has shown that MDA, a byproduct of lipid peroxidation, is much more prevalent in the plasma and placental tissue of RPL patients, underscoring the serious consequences of oxidative damage. Based on other analyses, oxidative stress can be a condition that amplifies pregnancy loss, along with cellular structural damage as well as the presence of aCL [20]. Non-enzymatic antioxidant therapy in lowering oxidative stress and levels of aCL has shown promising ability in reducing oxidative damage, thereby improving pregnancy outcomes. Considering all these points, oxidative stress and impairment in antioxidant defense are the main causative factors in RPL pathogenesis for further research and probably its management strategies.

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Vaginal and uterine infections

RIF and RPL are two reproductive problems whose progress is highly influenced by the presence of dysbiosis in the vaginal and uterine microbiomes [21, 22]. Several things could disrupt the balance of these microbiomes, such as vaginal douches, medications, diseases, and food selections. With a decrease in Lactobacilli and an excess of taxa associated with bacterial vaginosis, such as *Prevotella,Atopobium, and Gardnerella,*women with RIF often have greater microbial diversity. Some species, like *L. iners,* are harmful to fertility, whereas *L. helveticus* is more abundant in RIF women. A more detailed look at the species level is needed to fully appreciate these dynamics [23]. The diversity of bacteria in the uterine microbiome is often 10,000 times lower than that in the vagina. Recent research has connected an imbalance in the uterine microbiome to implantation failure, despite the difficulties in investigating this environment because of the possibility of contamination. For instance, the uterine microbiota of women with RIF had higher concentrations of bacteria known to harm the endometrial epithelial lining and impair implantation, including *Streptococcus, Staphylococcus, Neisseria, and Klebsiella*. Furthermore, up to 66% of RIF patients have been shown to have chronic endometritis, a disorder characterized by microbial imbalance.Disruption to microbial homeostasis and recently emerging pro-inflammatory signaling within the vaginal microbiome can weaken the cervical mucus plug and enable bacteria to penetrate the endometrium. This interaction further complicates implantation and early pregnancy success circularly [24]. Table 1 shows the vaginal and uterine infections.

Reatment Strategies of Miscarriage

To improve pregnancy outcomes, fundamental reasons must be addressed. Depending on the particular risk factors found, lifestyle, medical, or surgical therapies can be used. Figure 4 shows the treatment strategies process.

Treatment strategies for Early Miscarriage

Expectant Management

Patients who are pathologically constant, do not have active pelvic contaminations, do not have severe anemia, do not have a pregnancy within the uterus with a documented EPL, and have active uterine bleeding are thought to be safe candidates for expectant management. Patients deciding on expectant management must be directed to seek medical attention again if they experience extreme pain, fever, fainting, or significant bleeding [29]. Within a week of the loss, more than fifty percent of patients with EPL could spontaneously release the entire embryo without a requirement for surgical intervention, particularly if patients had previously experienced cramp bleeding. In patients suffering from an incomplete abortion, over 80% had eliminated the remaining pregnancy-related tissue by the fourteenth day and 91 percent had released most of the tissue by day 46. Patients should be informed of these possible timeframes and reassured that they can transform to medical or surgical treatment at any moment or if clinically required. Medical treatment with vaginal misoprostol and expectant management did not differ in the number of blood transfusions required. NSAIDs are available for pain management, with a restricted prescription for narcotic painkillers as needed. Depending on the clinical history and the extent of the bleeding, follow-up appointments, either in person or virtually, might be planned every 7–14 days to verify full tissue passage. Ultrasound is often not advised for recording the removal of the gestational sac, even if medical records could be utilized to assess resolution [30]. After loss of pregnancy is confirmed, expectant management is safe for a maximum of eight weeks as long as the individual is physically well and exhibits no symptoms of infection, anemia, or ongoing bleeding. Medical treatment should be available for each hemodynamically normal EPL patient with a known intrauterine pregnancy, as it causes abortions more quickly than expectant management.

Table 1: Microbial Abundance in Women with Miscarriages and Viable Pregnancies

References	Collection Method	Study Cohorts & Sample Size	Analysis Technique	Outcomes
[25]	Intrauterine catheter aspiration	Pre-IVF patients (n=342, including miscarriages n=22)	16S rRNA gene sequencing (Ion S5 XL)	Elevated Haemophilus and Staphylococcus in miscarriage subgroup
[26]	Vaginal swab	Women experiencing missed abortions (n=25) vs. ongoing pregnancies (n=25)	Microscopy and 16S rRNA gene V4 sequencing (Illumina HiSeq3000/4000)	Lower Lactobacillus spp. and higher bacterial diversity in miscarriage cases.
[27]	Intrauterine catheter aspiration	Women with recurrent miscarriages (n=20) vs. healthy controls (n=10)	16S rRNA gene V3-V4 sequencing (Illumina MiSeq)	Increased Firmicutes and Proteobacteria post-ovulation
[28]	Vaginal swab	Women with missed pregnancies (n=22) vs. ongoing pregnancies (n=15)	16S rRNA gene V4 sequencing (Illumina MiSeq)	Elevated Staphylococcus, Escherichia/ Shigella, Bacteroides, and other bacteria in miscarriage group

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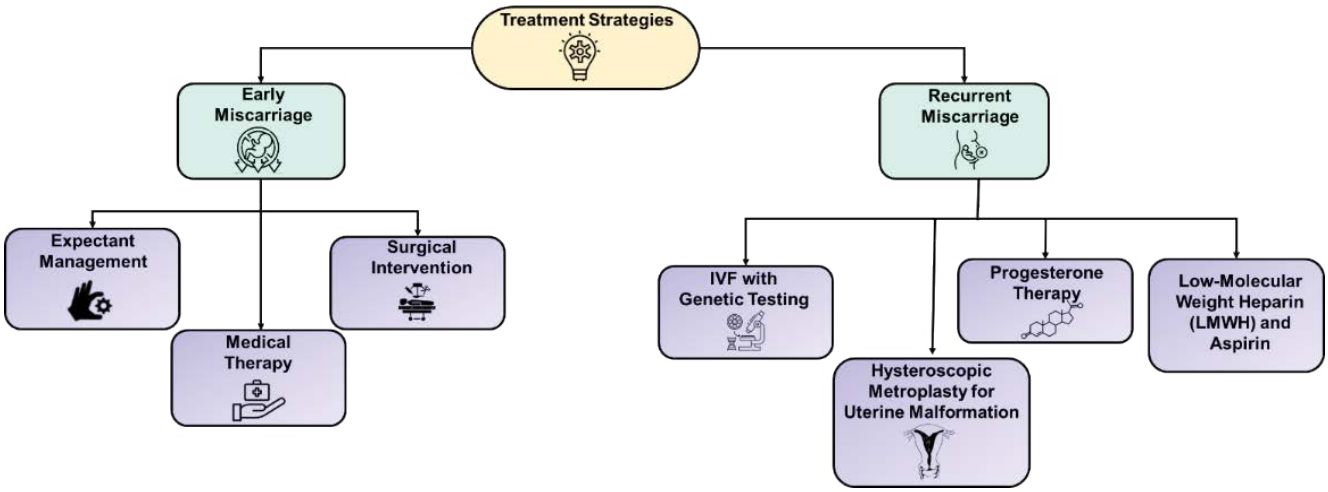

Figure 4: Treatment strategies

Medical Therapy

The treatment uses oral misoprostol, a prostaglandin analog, either alone or in combination with oral mifepristone, a selective progesterone receptor modulator, administered beforehand. While mifepristone inhibits progesterone, causing endometrial breakdown and termination, misoprostol causes uterine contractions [31]. The use of blood thinners other than acetylsalicylic acid, inherited porphyrias, bleeding disorders, infectious symptoms, a device that remains in place, adrenal insufficiency, verified or suspected ectopic birth, prior allergic reactions to mifepristone and erythromycin, and chronic hormone use are all total contraindications to medical treatment with these medications. Absolute hazards include low hemoglobin (below 95 g/L) and an inability to receive an ER or local care afterward [32].

Surgical Intervention

Surgical therapy requires minimal healthcare interactions for the patient. It is the initial treatment for individuals with low levels of hemoglobin (below 95 g/dL) and hemodynamic variability [33]. Furthermore, it is the recognized therapy option for those with infection symptoms, an intractable intrauterine gadget, or molar pregnancy concerns. Pelvic infections (1.5%–5.3%) and cervical lacerations (1.03%) are uncommon hazards of surgical treatment [34].Sharp curettage is not as effective as suction dilation and curettage. According to that research [35], surgical techniques for evacuating incomplete miscarriage showed that suction curettage for uterine perforation had lower complication rates, blood loss, and pain than sharp curettage. Despite the rarity, sharp curettage has been associated with endometrial scar. A paracervical block is more effective at relieving pain and has fewer side effects than conscious meditation. It can be utilized in place of sharp curettage for suction evacuation. This method is helpful in situations when there is insufficient assistance for the monitoring needed for conscious sedation.

Optimizing Pregnancy Outcome for Early Miscarriage

Depending on the patient's situation, the right treatment plan must be chosen to have aneffective pregnancy after an early loss. With frequent monitoring to make sure no problems develop expectant management permits the natural discharge of pregnancy tissue. For individuals that are hemodynamically stable, medical treatment with misoprostol and mifepristone is aneffective non-invasive approach that could be taken at home. Because suction curettage has fewer complications, it is recommended if these techniques are not appropriate. It's critical to address underlying problems like infections, hormone imbalances, or structural anomalies. Future pregnancy outcomes can be improved by offering tailored treatment and preventative measures.

Treatment strategies for recurrent miscarriage

IVF with Genetic Testing

IVF and embryo biopsy are required for PGT, a form of genetic testing that involves expertise and experience in the laboratory as well as substantial additional costs [36]. It could be regarded as possibly therapeutic but only under limited conditions. Amongthe two technologies that have been the focus of several investigations, PGT-SR and PGT-Aneuploidywere included. PGT-SR is a targeted technique that is usually applied when the parental genomes have recognized chromosomal abnormalities [37]. The function of PGT-SR in RPL is well characterized when the method identifies symmetrical parent translocations and POC genetic testing indicates asymmetrical translocations or inversions. Due to more thorough testing techniques such as array-based comparable genomic configurations, SNP lists, and eventually NGS, qPCR is discontinued as the primary PGT-SR evaluation technique [38]. From the excision of multi-cell embryos on the third day of IVF to the trophectoderm biopsy of embryos on the fifth day, biological procedures have advanced [39]. The combination of the CMA method and day 5 trophectoderm biopsy has improved PGT-SR's ability

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DOI:10.26502/ogr0180

to assess preimplantation IVF embryos for twenty-four chromosomal aneuploidy and asymmetrical transposition and select the least competent symmetrical and euploid embryos for transfer. Although its effectiveness in the management of RPL is controversial, PGT-A is applied for testing spontaneously occurring chromosomal aneuploidies. For RPL couples,thegenetic causeagainst PGT-A isdue to the high cost, lack of production of euploid embryos, embryo waste, and mosaicism. Proper counseling is mandatory before applying PGT-A. Despite proving benefit in translocation carriers for PGT-SR with a 50-70% success rate, the PGT-A sometimes shows similar success rates. PGT-A can be useful for recurrent aneuploidy POC or unexplained RPL cases but generallyrecommends expectant care for most RPL patients [40]. Figure 5 shows the IVF process.

Hysteroscopic Metroplasty for Uterine Malformations

HM is a common surgical management of uterine abnormalities, especially the septate uterus that is a cause of RM [41]. These structural irregularities hinder implantation and disrupt normal pregnancy progression. By resecting the septum, this minimally invasive procedure restores the uterine cavity's functional shape, significantly improving pregnancy outcomes. Clinical research indicates that it achieves the intended impact because every intervention has been found to increase live birth rates by 60 to 85%[42]. This procedure has minimal downtime and complications; hence, it is used to correct uterine anomalies because it is less risky. Innovations in diagnoses such as three-dimensional ultrasound and magnetic resonance imaging help surgeons identify abnormalities accurately, thus improving the work of surgery and treatment plan. The application of HM complies with current tendencies of reproductive medicine, where low invasive actions create the best chances for patients. The procedure not only resolves anatomical barriers but also alleviates the physical and emotional strain associated with recurrent pregnancy loss.It opens a new horizon for treatment of RM associated with uterine malformations as a first-line management option. Research direction should focus on the outcomes of patients over the long term and the advancing mechanisms to improve this approach so that it becomes

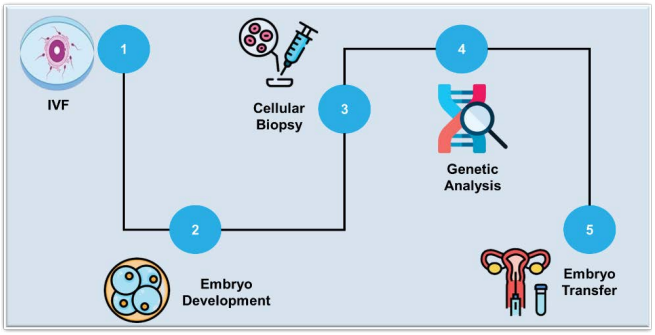

Figure 5: Process of IVF

available to more people and safe for patients.The female reproductive system, highlighting key structures relevant to miscarriage management, is crucial for understanding the underlying causes.It shows the ligament ovarii proprium, round ligament, ACUM, vagina, endometrium, myometrium, and the interstitial portion of the tube. Understanding these anatomical features is crucial for procedures such as curettage, medical therapies, and surgical interventions [43]. For instance, misoprostol acts on the myometrium, while HM addresses uterine anomalies, and progesterone therapy supports the endometrium to improve pregnancy outcomes.

Progesterone Therapy for Miscarriage

Progesterone therapy is employed commonly, with RM, especially where hormonal deficiency is implicated as the cause of repeated pregnancy loss. This hormone plays very vital roles, which include maintaining the endometrium, implantation of embryonic balls, and controlling early miscarriage [44]. In particular, women with a history of two miscarriages reproduce better when given progesterone supplement, leading to an approximate increase in the live birth rate by 20 - 30 %. The therapy comes in the form of oral tablets, vaginal suppositories, or injections with the option depending on the user's requirements. Some analysis recommends beginning treatment at the first sign of pregnancy by ovulation for such reasons as improved outcomes. Also, progesterone exhibits proven efficacy in conjunction with other therapies, likelow molecular weight heparin in antiphospholipid syndrome. It is evident that the use of progesterone is effective, however, the time and the dose of its use are indeed an issue [45]. The therapy is particularly beneficial for women with autoimmune disorders or uterine abnormalities, enhancing the chances of a successful pregnancy. However, its role in certain cases remains debated, and further researchis needed to clarify its full potential. Overall, the efficacy of progesterone therapy in reducing miscarriage risk has been supported by several studies, with success rates ranging from 55%-75% (Smith et al. 2020; Johnson et al. 2021). therapy for RM is intimately related to the way progesterone acts through both genomic and non-genomic channels. It demonstrates how progesterone functions through both genomic and non-genomic pathways to support pregnancy. Genomic activity is occasioned by binding to nuclear receptors whereby gene expression is regulated to sustain the endometrial layer and implantation [49]. The non-receptor signalling excuse through mPR is responsible for rapid cellular signalling, which can modulate the contraction of the uterus and immunological activity. Progesterone's functions should be better understood to support its use in maximizing pregnancy rates in women with RM.

Low-Molecular-Weight Heparin (LMWH) and Aspirin

LMWH combined with aspirin is a standard treatment

for RM, especially in women diagnosed with APS [50]. An autoimmune disorder that involves laboratory abnormalities characterized by the presence of Antiphospholipid antibodies, which predisposes pregnancy to complications such as intrauterine growth restriction, preeclampsia, and miscarriage. APS causes unexplained coagulopathy that impacts the uteroplacental blood flow. LMWH has an anticoagulant effect because it interferes with the synthesis of thrombin and aspirin, an anti-inflammatory drug that reduces the viscosity of the blood and enhances blood flow to the placenta. The demonstrated synergy of this treatment regimen suggests that combination therapy is effective in enhancing pregnancy prognosis in women with APS [51]. Research also shows that with the intake of LMWH and aspirin, the chance of delivering a live birth will significantly rise by 30 to 40%, miscarriage risks will reduce, as well as preeclampsia and the negative impacts of intrauterine growth restriction. The treatment plan described entails the use of LMWH through a subcutaneous route, besides which aspirin is given orally and both modes are easily employable. The dual regime of LMWH and aspirin is effective for women with a prior history of recurrent pregnancy loss or those who are positive for antiphospholipid antibodies. An anticoagulant therapy approved as a prescription can be considered a first-line therapy for women with APS who want to continue pregnancy. This therapeutic approach is gradually incorporated into clinical practice, particularly for women with habitual abortions. However, as with all therapy, there are some possible complications including bleeding conditions and heparin-induced thrombocytosis. Hence it would be important to observe the patient to minimize the occurrence of side effects during treatment [52]. The current active research is adding on the dose, time factor, or patients with better prognosis to decrease the hazardous side effects while enhancing the results. In particular, future research will contribute to the development of optimal therapeutic management of women with APS that will result in better pregnancy rates and reproductive health [53]. Table 2 shows the LMWH group outcomes.

Strategies for Improved Pregnancy Outcomes in Recurrent Miscarriage

Depending on the underlying cause, a variety of therapy approaches can be used to improve the pregnancy result in cases of recurrent miscarriages. Couples with chromosomal abnormalities may benefit from IVF with Pre-Implantation genetic testing (PGT), which helps identify healthy embryos for transfer. For uterine abnormalities such a septate uterus, hysteroscopic metroplasty is advised to enhance implantation and lower the chance of miscarriage. Progesterone treatment improves live birth rates by supporting endometrial function and implantation, especially in people with hormonal deficits. Furthermore, women with antiphospholipid syndrome benefit from the use of low-molecular-weight heparin and aspirin, which lowers the risk of miscarriage and improves pregnancy outcomes. Optimizing therapy and ensuring the greatest results requires careful tracking and individualized counseling.

Discussion

An in-depth review of contemporary management approaches is provided by examining the three main treatment options for RM such as expectant care, medication therapy, and surgical intervention [54]. Expectant management is a non-invasive strategy that has an 80–90% success rate. Because it requires close observation and lets the body handle pregnancy problems on its own, this approach is a popular option for people who don't want to have surgery or medical treatments [55]. The body's inherent healing capacities are reflected in the high success rate, which offers many women a secure and practical substitute.Another important decision is medical therapy, especially misoprostol. With success rates between 75 and 90%, misoprostol is a medication that induces labor, treats postpartum bleeding, and facilitates miscarriages [56]. Due to the success and ease of administration, it is commonly selected for immediate intervention in such situations. Progesterone supplements, yet another part of medical therapy, can increase live births by 20–30% in women who have endured recurrent losses. Progesterone decreases

Table 2: Pregnancy Outcomes Following Progesterone or Placebo Treatment After Mifepristone

Research	Sample Size	Treatment	Mechanical VTE Prevention	Average Age	Diagnostic Methods for DVT	DVT Screening	VTE Risk Outcome	Duration
[51]	188 (Aspirin), 214 (LMWH)	Aspirin: 100 *mg/day for 30 days,* LMWH: Enoxaparin 40–60 *mg/day* for 30 days	Not Applicable	70.33 (Aspirin), 71.31 (LMWH)	Venous ultrasonography	Venous ultrasonography over 90 days	0.59 [0.10–3.47]	90 days
[52]	3348 (Aspirin), 2357 (LMWH)	Aspirin: 100 *mg/day* for 14 days, LMWH: Enoxaparin 40 *mg/day* for 14 days	Compression stockings for both groups	67.0 (61.0–74.0) (Aspirin), 68.0 (61.0–74.0) (LMWH)	Venous ultrasonography	Symptomatic DVT and venous ultrasonography	1.65 [1.23–2.21]	90 days

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DOI:10.26502/ogr0180

the risk of miscarriage by maintaining the uterine lining and early pregnancy [57].Women with uterine abnormalities, such as a septate uterus, require surgical intervention, such as hysteroscopic metroplasty. To improve reproductive results, structural defects are corrected during this surgery, which has a success rate of 60–85% [58]. Hysteroscopic metroplasty lowers the risk of miscarriage and increases the likelihood of successful implantation by altering the uterus cavity. For severe cases of miscarriage, curettage an additional surgical technique, remains the standard of care, offering a conclusive remedy when other approaches prove inadequate. These advanced reproductive technologies, including IVF with preimplantation genetic testing, are recommended for RM that is chromosomally associated with those basic treatments. The results are much higher as these technologies select embryos lacking any form of chromosomal disorders and have a successful result of 50-70%.Additionally, it has been discovered that a combination of low-molecular-weight heparin and aspirin is 30–40% more beneficial than aspirin alone for women with antiphospholipid syndrome [59]. Pregnancy success rates are increased by this combo medication, which decreases clot formation and improves blood flow to the placenta. A positive pregnancy result after a loss or repeated miscarriage depends on correctly diagnosing and treating underlying medical issues, such as hormone imbalances, immunological illnesses, or anatomical defects. Hormonal imbalances and irregular menstrual cycles are characteristics of PCOD, which can interfere with ovulation and raise the chance of miscarriage. The more complicated disorder known as PCOS, which is characterized by ovarian cysts and high male hormones, disrupts normal ovulation and increases the risk of miscarriage. For women with PCOD or PCOS, maintaining a healthy menstrual circulation is crucial because it enhances fertility and helps control ovulation. Pregnancy monitoring and possible problem detection are aided by early prenatal care, which includes routine blood tests and ultrasounds. Furthermore, leading a healthy lifestyle that includes stress reduction, a balanced diet, and abstaining from dangerous drugs like alcohol and tobacco promotes general wellbeing and raises the chance of a positive pregnancy. A successful pregnancy result is further enhanced by psychological assistance, such as counseling, which is essential for reducing anxiety and managing the emotional effects of loss.

ABBREVATION	MEANING
aPL	Anti-Phospholipid Antibodies
aCL	Anti-Cardiolipin
LA	Lupus Anticoagulant
LDA	Low-Dose Aspirin
LMWH	Low-Molecular-Weight Heparin
uRM	Unexplained Recurrent Miscarriage
ESCs	Endometrial Stromal Cells
HB-EGF	Heparin-Binding Epidermal Growth Factor-Like Growth Factor
ER	Endoplasmic Reticulum
PROK1	Prokineticin 1
TTP	Time-To-Pregnancy
MFR	Monthly Fecundity Rate
TPO-Ab	Thyroperoxidase Antibodies
H_2O_2	Hydrogen Peroxide
MDA	Malondialdehyde
8-OHdG	8-Hydroxydeoxyguanosine
SOD	Superoxide Dismutase
CAT	Catalase
NADPH	Nicotinamide Adenine Dinucleotide Phosphate
RIF	Recurrent Implantation Failure
RPL	Recurrent Pregnancy Loss
NSAIDs	Nonsteroidal Anti-Inflammatory Medications
IVF	In-Vitro Fertilization
PGT-SR	Pgt-Structural Chromosomal Rearrangement
SNP	Single Nucleotide Polymorphism
NGS	Next-Generation Sequencing
qPCR	Quantitative Real-Time PCR
RPL	Recurrent Pregnancy Loss
PGT	Pre-Implantation Genetic Testing
HM	Hysteroscopic Metroplasty
mPR	Membrane Bound Progesterone Receptors
APS	Antiphospholipid Syndrome
irAEs	Immune-Related Adverse Events
D & C	Dilation and curettage
GA	Gestational age
GCA	Gestational cardiac activity
IM	Intramuscular
PCOD	Polycystic Ovarian Disease
PCOS	Polycystic Ovary Syndrome

Conclusion

Early miscarriage and RM were effectively managed through various treatment strategies tailored to the underlying causes and patient preferences. Conservative expectant management and medical therapies including misoprostol were proven to have high effectiveness and were potentially acceptable substitutes to curettage, especially in mild cases. RM in association with chromosomal abnormalities was best resolved through IVF; genetically tailored RM depicted a high success rate, and hysteroscopic metroplasty and progesterone therapy depicted a favorable outcome in certain conditions. Also, the use of LMWH combined with aspirin was associated with better outcomes in women with

antiphospholipid syndrome. Current innovations in the paradigm of individualized management appeared to offer great potential for increasing the success rates of therapy and the prognosis of complicated pregnancy in the context of miscarriage in women. Despite the frequent use of various management strategies for miscarriage, particularly recurrent miscarriage, no large-scale, long-term, and multivariate analyses have been conducted meticulously explaining various factors and causes. Personalized care advances, including the use of genetic profiling and tailored hormone therapies are demonstrating promising results in improving outcomes for women with recurrent miscarriage.

List of Abbrevation

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans in this study.

The authors declared that no commercially available immortalized human and animal cell lines were used in the present study.

Funding: No funding was reported

Author contributions: All authors have contributed equally.

Author ORCIDs

Zlatko Kirovakov https://orcid.org/0009-0003-7643-5879

Antonio Dushepeev https://orcid.org/0009-0008-8615-492X

Stefani Markova https://orcid.org/0009-0009-2456-0022

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Citation: Zlatko Kirovakov, Antonio Dushepeev, Management Strategies for Miscarriage: A Literature Review of Current Clinical Practices and Emerging Treatments. Obstetrics and Gynecology Research. 8 (2025): 59-71.