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MATERNAL COMPLICATIONS IN MISSED MISCARRIAGE – A LITERATURE REVIEW

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Abstract. *Background and objective: Missed miscarriage is an important form of early pregnancy loss that may be associated with maternal complications. The aim of this review was to summarize the main maternal complications associated with missed miscarriage and to emphasize the importance of timely diagnosis, individualized management, and appropriate preconception care. Materials and methods: A narrative review of national and international literature was performed, focusing on maternal morbidity, complications associated with medical and surgical management, etiological factors, and reproductive implications of missed miscarriage. Results: The main maternal complications identified were hemorrhage, anemia, retained products of conception, intrauterine infection, and complications associated with uterine evacuation. Severe complications, including sepsis, hemorrhagic shock, severe anemia, and coagulation disorders, are less frequent but may occur, particularly when diagnosis or treatment is delayed. Individualized selection of expectant, medical, or surgical management is important for reducing maternal morbidity. Histopathological examination of trophoblastic and placental tissues may contribute to elucidating the mechanisms underlying pregnancy loss. Preconception assessment is also important in women with a history of missed miscarriage. Conclusions: Early diagnosis, timely management of complications, individualized treatment, and adequate preconception care are key components in the management of missed miscarriage. Further studies specifically addressing missed miscarriage are needed, as a substantial proportion of recent literature evaluates this condition together with other forms of early pregnancy loss.*

Keywords: *anemia, early pregnancy loss, hemorrhage, infection, maternal complications, missed miscarriage, retained products of conception.*

Introduction

Missed miscarriage represents an important form of early pregnancy loss and is characterized by cessation of embryonic or fetal development without immediate expulsion of the products of conception. Its medical significance is determined not only by its relatively high frequency, but also by its potential physical, reproductive, and psychosocial consequences for women [11].

The etiology of missed miscarriage is complex and multifactorial. Genetic, endocrine, infectious, immunological, anatomical, medical, social, and environmental factors may be involved. The Moldovan medical literature has addressed missed miscarriage from several perspectives, including its medical-social characteristics, risk factors, morphological aspects, and implications for subsequent reproductive health [6, 7, 9].

From a medical-social perspective, missed miscarriage should not be regarded solely as an isolated obstetric event. It may influence maternal health, subsequent reproductive prognosis, and psychological well-being. Consequently, management should include prevention and identification of risk factors, early diagnosis, appropriate treatment, and individualized follow-up.

Recent international literature frequently uses the broader term early pregnancy loss, which includes several forms of early pregnancy failure, including missed miscarriage. Therefore, some of the evidence regarding maternal complications presented in the literature refers to early pregnancy loss as a broader category. This represents an important limitation when interpreting data specifically for missed miscarriages.

Etiological Aspects and Risk Factors

The etiology of missed miscarriage is multifactorial. Paladi and Mihalcean emphasized the role of genetic, endocrine, infectious, and immunological factors, together with social and environmental influences [3, 8, 10]. The interaction of these factors means that identification of a single causal mechanism is not always possible.

Morphological examination of trophoblastic and placental tissues may provide additional information regarding the mechanisms responsible for intrauterine death of the conceptus. Mihalcean highlighted the value of morphological examination of these structures in identifying pathological changes that may contribute to establishing the cause of pregnancy loss [9]. Thus, tissue examination following uterine evacuation may represent a useful component of the diagnostic assessment in selected cases.

The medical-social aspects of missed miscarriage have also been analyzed in the national literature [6, 7]. These studies emphasize the importance of considering women's general health status, reproductive history, and sociodemographic characteristics. A comprehensive evaluation may contribute to identifying factors potentially associated with recurrence.

Tabuica and Mihalcean analyzed risk factors associated with missed miscarriage and emphasized the importance of medical history and identification of maternal conditions associated with this pathology [11]. From a preventive perspective, identification of potentially modifiable factors may allow appropriate assessment and management before a subsequent pregnancy.

Preconception care is particularly relevant for women with a history of missed miscarriage. Such an approach provides an opportunity to evaluate maternal health, identify potentially modifiable risk factors, and establish an individualized plan for a subsequent pregnancy [5].

Hemorrhagic Complications

Hemorrhage represents one of the most important maternal complications associated with pregnancy loss. The severity of bleeding may range from limited blood loss to clinically significant hemorrhage accompanied by anemia, hemodynamic instability, and the need for urgent medical intervention.

In missed miscarriage, retained products of conception may be associated with persistent bleeding and may require medical or surgical evacuation of the uterine cavity. Timely diagnosis and appropriate management are therefore important components of preventing progression to complicated forms of pregnancy loss.

Benson et al. evaluated complications associated with early pregnancy loss management, including hemorrhage requiring transfusion, intrauterine infection, and the need for subsequent uterine procedures [2]. Their findings emphasize the importance of selecting a management strategy according to the clinical condition of the patient.

The maternal morbidity associated with pregnancy loss was also demonstrated by Etuk et al. in a study of 4,798 women experiencing pregnancy loss before 28 weeks of gestation. Among these women, 700 experienced at least one complication, with hemorrhage representing one of the important reported complications [4].

Severe hemorrhage may result in significant anemia and, in selected cases, may require blood transfusion and urgent intervention. Consequently, assessment of bleeding severity and maternal hemodynamic status is an essential component of clinical management.

Retained Products of Conception and Incomplete Evacuation

Retained products of conception constitute another important clinical concern following pregnancy loss. Incomplete evacuation of the uterine cavity may be associated with persistent vaginal bleeding, abdominal or pelvic pain, and an increased risk of infection. Additional therapeutic intervention may be necessary when complete evacuation is not achieved.

Management options for missed miscarriage include expectant, medical, and surgical approaches. The choice of management depends on the clinical condition of the woman, the presence of complications, and individual clinical characteristics.

For hemodynamically stable patients, medical management represents an important alternative to surgical intervention. Benson et al. analyzed outcomes of medical management of early pregnancy loss in 31,977 patients and reported that treatment with mifepristone followed by misoprostol was associated with a lower need for subsequent uterine aspiration compared with misoprostol alone: 10.5% versus 14.0%, respectively [1].

These findings suggest that the effectiveness of the selected medical regimen may influence the probability of requiring subsequent uterine procedures. Nevertheless, the treatment strategy should be individualized according to the patient's clinical condition and preferences, where clinically appropriate.

Surgical management may be indicated in cases of significant hemorrhage, persistent retained products of conception, or other clinical circumstances requiring rapid uterine evacuation. The therapeutic objective is to achieve complete evacuation while minimizing maternal morbidity.

Infectious Complications

Intrauterine infection represents a potentially serious complication of pregnancy loss. The presence of retained products of conception and incomplete evacuation may contribute to an increased risk of infection. When infection is not recognized and treated promptly, the process may progress from localized infection to systemic complications, including sepsis.

Infectious mechanisms have been identified among the factors potentially involved in missed miscarriage in the Moldovan literature [7, 10]. Morphological examination of trophoblastic and placental tissues may also provide information regarding pathological changes associated with intrauterine death of the conceptus [9].

The inflammatory component of reproductive pathology has also been addressed in studies of women with infertility. Burac et al. reported inflammatory endometrial changes and the presence of plasma cells in women with primary infertility [3]. Although this study did not directly investigate women with missed miscarriage, its findings indicate the potential importance of endometrial inflammatory changes in reproductive pathology and support the need for further investigation of this aspect.

The clinical importance of infectious complications is supported by data regarding pregnancy loss-associated maternal morbidity. Etuk et al. reported severe complications including sepsis among women with pregnancy loss [4]. These findings emphasize the importance of early recognition and treatment of infection in women experiencing pregnancy loss.

Complications of Surgical Management

Surgical evacuation of the uterine cavity represents an effective treatment option but, as with any invasive procedure, may be associated with complications. These include hemorrhage, infection, cervical trauma, and uterine perforation.

The decision to use surgical management should therefore take into consideration the woman's clinical condition, the severity of bleeding, the presence of retained products of conception, and the potential risks and benefits of alternative management strategies.

In certain clinical situations, surgical management provides the most rapid method of controlling significant hemorrhage or removing retained tissue. Therefore, procedural risks should be assessed in relation to the expected therapeutic benefits and the risks associated with continued retention of products of conception or alternative treatment.

Medical management may reduce the need for subsequent surgical intervention in appropriately selected patients. The comparative findings reported by Benson et al. regarding mifepristone plus misoprostol and misoprostol alone illustrate the relevance of treatment efficacy to the probability of subsequent uterine aspiration [1].

Severe Maternal Complications

Although most cases of missed miscarriage can be managed without severe maternal morbidity, serious complications may occur. These include severe anemia, hemorrhagic shock, sepsis, and coagulation disorders.

Etuk et al. investigated maternal morbidity and mortality associated with pregnancy loss before 28 weeks of gestation in Nigeria. Among the women included in the study, 14.6% experienced complications and mortality was 2.1%. Severe clinical manifestations included hemorrhage, severe anemia, sepsis, shock, and coagulation disorders [4].

These results should be interpreted in the context of the population and healthcare system in which the study was conducted. Nevertheless, they demonstrate that pregnancy loss may become an important cause of maternal morbidity when diagnosis or treatment is delayed or when access to appropriate medical care is limited.

From a clinical perspective, the prevention of severe complications requires early recognition of significant bleeding, infection, retained products of conception, and maternal deterioration. Individualized management and timely intervention remain essential components of care.

Importance of Prevention and Preconception Care

The prevention of complications associated with missed miscarriage should not be limited to the acute episode. Assessment after pregnancy loss and appropriate preconception care are particularly relevant for women with a previous history of missed miscarriage.

Mihalcean analyzed risk factors and preconception management in women with a history of missed miscarriage and emphasized the importance of comprehensive patient assessment [5]. Preconception care provides an opportunity to identify potentially modifiable risk factors and optimize maternal health before a subsequent pregnancy.

The broader reproductive significance of missed miscarriage was also highlighted in the analysis of Mihalcean published in 2026, which considered missed miscarriage within the structure of reproductive losses in the context of declining birth rates and increasing infertility [8]. This perspective emphasizes that missed miscarriage should be considered not only as an isolated obstetric event but also as a condition with implications for reproductive health.

An individualized preconception approach may therefore include assessment of the woman's medical and reproductive history, evaluation of relevant risk factors, and correction or management of potentially modifiable conditions. Such an approach may contribute to optimizing subsequent reproductive outcomes.

Conclusions

Missed miscarriage is a multifactorial condition with important implications for maternal and reproductive health. The reviewed literature indicates that the principal maternal complications include hemorrhage, anemia, retained products of conception, intrauterine infection, and complications associated with uterine evacuation procedures.

Hemorrhage represents one of the most important complications and may range from limited bleeding to severe hemorrhage requiring transfusion and urgent intervention. Retained products of conception may contribute to persistent bleeding and infection, while surgical evacuation, although effective, is associated with potential procedural risks.

Severe complications, including sepsis, hemorrhagic shock, severe anemia, and coagulation disorders, are less frequent but may have major clinical consequences. Their occurrence emphasizes the importance of early diagnosis, appropriate monitoring, and timely treatment.

Morphological examination of trophoblastic and placental tissues represents an additional diagnostic tool that may contribute to understanding the mechanisms responsible for intrauterine death of the conceptus [9]. Integration of clinical, medical-history, and histopathological information may facilitate a more comprehensive assessment of individual cases.

The Moldovan literature emphasizes the multifactorial nature of missed miscarriage and the importance of genetic, endocrine, infectious, immunological, and medical-social factors [6, 7, 10, 11]. Contemporary international studies provide additional evidence regarding maternal complications and the effectiveness of different management strategies [1, 2, 4].

Preconception care in women with a history of missed miscarriage represents an important component of reproductive healthcare. Identification and management of potentially modifiable risk factors may contribute to optimization of maternal health and subsequent reproductive outcomes [5].

In conclusion, the management of missed miscarriage should focus on prevention, early recognition, and prompt treatment of maternal complications through an individualized approach based on comprehensive clinical assessment. Further prospective studies specifically addressing missed miscarriage are required, as a substantial proportion of contemporary evidence groups this condition together with other forms of early pregnancy loss.

REFERENCES

1. Benson, L.S., Gunaje, N., Holt, S.K., Gore, J.L., Dalton, V.K. Outcomes After Early Pregnancy Loss Management With Mifepristone Plus Misoprostol vs Misoprostol Alone. *JAMA Network Open*. 2024;7(10):e2435906.
2. Benson, L.S., Holt, S.K., Gore, J.L., et al. Early Pregnancy Loss Management in the Emergency Department vs Outpatient Setting. *JAMA Network Open*. 2023;6(3):e232639.
3. Burac, M., Corolcova, N., Mihalceanu, L., Cotelea, V. Aprecierea plasmocitelor în endometrul femeilor cu infertilitate primară. In: *Sănătate Publică, Economie și Management în Medicină*. 2024;1(98 S):60.
4. Etuk, S.J., et al. Maternal morbidity and death associated with pregnancy loss before 28 weeks in Nigeria. *BJOG*. 2024;131(Suppl 3):20–29.
5. Mihalcean, L. Factorii de risc și conduita preconcepțională a femeilor cu sarcină oprită în evoluție în anamneză. Teză de doctor în științe medicale. Chișinău: Centrul Editorial-Poligrafic Medicina; 2010.
6. Mihalcean, L. Sarcina oprită în evoluție: aspecte medico-sociale. Teză de doctor în științe medicale. Chișinău; 2010.
7. Mihalcean, L. Sarcina oprită în evoluție (Reviul literaturii). In: *Analele Științifice ale USMF „N. Testemițanu”*. 2012;5(13):87–95.
8. Mihalcean, L. Sarcina stagnată în structura pierderilor reproductive în contextul scăderii natalității și creșterii infertilității. *Buletinul Academiei de Științe a Moldovei. Științe Medicale*. 2026;1(84):313–319.
9. Mihalcean, L. Valoarea examenului morfologic al derivatelor trofoblastului/placentei în determinarea cauzei morții intrauterine a produsului de concepție. In: *Analele Științifice ale USMF „N. Testemițanu”*. 2010;5(11):65–72.
10. Paladi, G., Mihalcean, L. Sarcina oprită în evoluție: aspecte medico-sociale. *Reviul literaturii. Buletinul Academiei de Științe a Moldovei. Științe Medicale*. 2008;2:34–41.
11. Tabuica, U., Mihalcean, L. Estimarea factorilor de risc pentru survenirea sarcinii stagnate în evoluție. *Buletinul Academiei de Științe a Moldovei. Științe Medicale*. 2009;2(21):246–252.

REFERENCES

1. Benson L.S., Gunaje N., Holt S.K., Gore J.L., Dalton V.K. Outcomes After Early Pregnancy Loss Management With Mifepristone Plus Misoprostol vs Misoprostol Alone. *JAMA Network Open*. 2024;7(10):e2435906.
2. Benson L.S., Holt S.K., Gore J.L., et al. Early Pregnancy Loss Management in the Emergency Department vs Outpatient Setting. *JAMA Network Open*. 2023;6(3):e232639.
3. Burac M., Corolcova N., Mihalceanu L., Cotelea V. Aprecierea plasmocitelor în endometrul femeilor cu infertilitate primară. In: *Sănătate Publică, Economie și Management în Medicină*. 2024;1(98 S):60.
4. Etuk S.J., et al. Maternal morbidity and death associated with pregnancy loss before 28 weeks in Nigeria. *BJOG*. 2024;131(Suppl 3):20–29.
5. Mihalcean L. Factorii de risc și conduita preconcepțională a femeilor cu sarcină oprită în evoluție în anamneză. Teză de doctor în științe medicale. Chișinău: Centrul Editorial-Poligrafic Medicina; 2010.
6. Mihalcean L. Sarcina oprită în evoluție: aspecte medico-sociale. Teză de doctor în științe medicale. Chișinău; 2010.
7. Mihalcean L. Sarcina oprită în evoluție (Reviul literaturii). In: *Analele Științifice ale USMF „N. Testemițanu”*. 2012;5(13):87–95.
8. Mihalcean L. Sarcina stagnată în structura pierderilor reproductive în contextul scăderii natalității și creșterii infertilității. *Buletinul Academiei de Științe a Moldovei. Științe Medicale*. 2026;1(84):313–319.
9. Mihalcean L. Valoarea examenului morfologic al derivatelor trofoblastului/placentei în determinarea cauzei morții intrauterine a produsului de concepție. In: *Analele Științifice ale USMF „N. Testemițanu”*. 2010;5(11):65–72.
10. Paladi G., Mihalcean L. Sarcina oprită în evoluție: aspecte medico-sociale. *Reviul literaturii. Buletinul Academiei de Științe a Moldovei. Științe Medicale*. 2008;2:34–41.
11. Tabuica U., Mihalcean L. Estimarea factorilor de risc pentru survenirea sarcinii stagnate în evoluție. *Buletinul Academiei de Științe a Moldovei. Științe Medicale*. 2009;2(21):246–252.

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МАТЕРИНСКИЕ ОСЛОЖНЕНИЯ ПРИ НЕРАЗВИВАЮЩЕЙСЯ БЕРЕМЕННОСТИ — ОБЗОР ЛИТЕРАТУРЫ

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Аннотация. *Актуальность и цель:* Неразвивающаяся беременность является важной формой ранней потери беременности и может сопровождаться различными материнскими осложнениями. Целью настоящего обзора было обобщение основных материнских осложнений, связанных с неразвивающейся беременностью, а также оценка значения своевременной диагностики, индивидуализированного лечения и адекватной прегравидарной подготовки. *Материалы и методы:* Проведен нарративный обзор национальной и международной литературы, посвященной материнской заболеваемости, осложнениям медикаментозного и хирургического лечения, этиологическим факторам и репродуктивным последствиям неразвивающейся беременности. *Результаты:* Основными материнскими осложнениями являются кровотечение, анемия, задержка продуктов зачатия, внутриматочная инфекция и осложнения, связанные с эвакуацией содержимого полости матки. Тяжелые осложнения, включая сепсис, геморрагический шок, выраженную анемию и нарушения свертывания крови, встречаются реже, однако могут развиваться при поздней диагностике или несвоевременном лечении. Индивидуальный выбор выжидательной, медикаментозной или хирургической тактики имеет важное значение для снижения материнской заболеваемости. Морфологическое исследование трофобластических и плацентарных тканей может способствовать уточнению механизмов внутриутробной гибели эмбриона или плода. Важное значение имеет также прегравидарная подготовка женщин с анамнезом неразвивающейся беременности. *Выводы:* Ранняя диагностика, своевременное лечение осложнений, индивидуальный выбор метода лечения и адекватная прегравидарная подготовка являются ключевыми компонентами ведения неразвивающейся беременности. Необходимы дальнейшие исследования, специально посвященные неразвивающейся беременности, поскольку значительная часть современной литературы рассматривает ее в составе других форм ранней потери беременности.

Ключевые слова: анемия, инфекция, кровотечение, материнские осложнения, неразвивающаяся беременность, ранняя потеря беременности, задержка продуктов зачатия.