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E: ndmuz@mail.ru
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RECURRENT PREGNANCY LOSS

Kamalova Dilafruz Doniyorovna https://orcid.org/0009-0005-2859-1556
e-mail: dilafruz1939@gmail.com

Samarkand State Medical University Uzbekistan, Samarkand, st. Amir Temur 18, Tel: +99818 66 2330841 E-mail: sammu@sammu.uz

✓ ***Resume***

Recurrent pregnancy loss is one of the areas where reproductive medicine continues to face major problems, with recurrent gestational failures that often occur despite an extensive clinical investigation. Defined as the loss of two or more consecutive pregnancies before reaching foetal viability, this disorder places a significant physical and psychological burden on affected women, thus creating a significant amount of diagnostic and therapeutic uncertainty. Although many etiological factors have been discovered, a significant number of cases are still idiopathic, pointing to the complexity of the underlying mechanisms. This study aimed to assess the clinical characteristics, contributing factors and pregnancy outcomes in women with recurrent pregnancy loss under the management of a tertiary medical centre in Samarkand. An observational design was used for this study. 89 women were enrolled for the study period (September 2023 -- September 2025). Comprehensive assessment included reproductive history assessment, endocrine and immune assessment, uterine imaging and prospective monitoring of future pregnancies. Management strategies were individualised and were based on identified risk factors, as well as current clinical guidelines. The results showed that endocrine and immune-related abnormalities were the most commonly found contributors; however, there was no single factor that was consistently found to predict the outcome of pregnancy. Importantly, a significant proportion of women had successful pregnancies during follow-up, including women who had no identifiable etiological factors. This finding emphasises the dynamic nature of recurrent pregnancy loss, and that prognosis should not be thought of as fixed based solely on the reproductive history to date.

Keywords: Recurrent Pregnancy Loss; Miscarriage; Infertility P

TAKRORIY HOMILA YO‘QOTISH

Kamalova Dilafruz Doniyorovna https://orcid.org/0009-0005-2859-1556

Samarqand davlat tibbiyot universiteti O‘zbekiston, Samarqand, st. Amir Temur 18, Tel: +99818 66 2330841 E-mail: sammu@sammu.uz

✓ ***Rezyume***

Takroriy homila yo‘qotish reproduktiv tibbiyotda hanuzgacha muhim muammolardan biri bo‘lib qolmoqda, chunki takroran gestatsion muvaffaqiyatsizliklar ko‘pincha keng qamrovli klinik tekshiruvlarga qaramasdan ham yuz beradi. Ikki yoki undan ortiq ketma-ket homiladorlikning fetal hayotiylik davriga yetmasdan yo‘qotilishi sifatida ta’riflanadigan ushbu holat ayollarda jiddiy jismoniy va ruhiy bosimni yuzaga keltiradi hamda diagnostika va davolash borasida muhim noaniqliklarni keltirib chiqaradi. Ko‘plab etiologik omillar aniqlangan bo‘lsa-da, holatlarning sezilarli qismi hanuz idiopatik bo‘lib qolmoqda, bu esa asosiy mexanizmlarning murakkabligini ko‘rsatadi. Ushbu tadqiqotning maqsadi Samarqanddagi uchlamchi tibbiyot markazida kuzatuv ostida bo‘lgan takroriy homila yo‘qotish holatiga ega ayollarda klinik xususiyatlar, omillarning ulushi hamda homiladorlik natijalarini baholashdan iborat bo‘ldi. Tadqiqotda kuzatuv (observatsion) dizayni qo‘llanildi. Tadqiqot davrida (2023-yil sentyabr - 2025-yil sentyabr) 89 nafar ayol tekshiruvga jalb qilindi. Kompleks baholash reproduktiv anamnezni tahlil qilish, endokrin va immun tekshiruvlar, bachadonning tasviriy diagnostikasi hamda keyingi homiladorliklarni istiqbolli

tarzda kuzatishni o‘z ichiga oldi. Davolash strategiyalari aniqlangan xavf omillariga va mavjud klinik tavsiyalarga asoslangan holda individuallashtirildi. Natijalarga ko‘ra, endokrin va immun tizim bilan bog‘liq o‘zgarishlar eng ko‘p uchragan omillar sifatida qayd etildi, biroq homiladorlik natijasini izchil tarzda bashorat qila oladigan yagona omil aniqlanmadi. Muhim jihati shundaki, kuzatuv davomida ayollarning sezilarli qismi muvaffaqiyatli homiladorlikka erishdi, shu jumladan etiologik omillar aniqlanmagan ayollar ham. Ushbu holat takroriy homila yo‘qotishning dinamik xususiyatga ega ekanini ko‘rsatadi hamda prognoz faqat hozirgacha bo‘lgan reproduktiv anamnez asosida qat’iy baholanmasligi kerakligini ta’kidlaydi.

Kalit so‘zlar: Takroriy homila yo‘qotish; Homila tushishi; Bepushtlik

ПОВТОРНЫЕ ПОТЕРИ БЕРЕМЕННОСТИ

Камалова Дилафруз Дониеровна https://orcid.org/0009-0005-2859-1556

Самаркандский государственный медицинский университет Узбекистан, г.Самарканд,
ул. Амира Темура 18, Тел: +99818 66 2330841 E-mail: sammu@sammu.uz

✓ ***Резюме***

Повторные потери беременности остаются одной из наиболее сложных проблем современной репродуктивной медицины, поскольку повторяющиеся гестационные неудачи нередко наблюдаются даже после проведения расширенного клинического обследования. Данное состояние определяется как потеря двух или более последовательных беременностей до достижения плодом жизнеспособности. Оно вызывает значительную физическую и психологическую нагрузку у женщин и формирует выраженную диагностическую и терапевтическую неопределённость. Несмотря на выявление множества этиологических факторов, значительная доля случаев по-прежнему остаётся идиопатической, что отражает сложность и многоуровневость патогенетических механизмов.

Целью настоящего исследования было оценить клинические особенности, возможные факторы риска и исходы беременности у женщин с повторными потерями беременности, наблюдавшихся в условиях третичного медицинского центра Самарканда. Исследование выполнено в формате наблюдательного (обсервационного) дизайна. В течение периода исследования (сентябрь 2023 - сентябрь 2025) в работу были включены 89 женщин. Комплексная оценка включала анализ репродуктивного анамнеза, эндокринологическое и иммунологическое обследование, визуализацию матки и проспективное наблюдение последующих беременностей. Стратегии ведения подбирались индивидуально в зависимости от выявленных факторов риска и в соответствии с действующими клиническими рекомендациями. Результаты показали, что эндокринные и иммунные нарушения являлись наиболее часто выявляемыми факторами, однако не было обнаружено единственного предиктора, который бы стабильно определял исход беременности. Важно отметить, что в процессе наблюдения значительная часть женщин достигла успешной беременности, включая пациенток без выявленных этиологических причин. Этот факт подчёркивает динамический характер повторных потерь беременности и свидетельствует о том, что прогноз не должен рассматриваться как фиксированный только на основании предыдущего репродуктивного анамнеза.

Ключевые слова: Повторные потери беременности; Самопроизвольный выкидыш; Бесплодие

Relevance

Recurrent pregnancy loss is not only a clinical diagnosis but a disease which has a significant biological and emotional burden to women and their families. Defined as the loss of two or more pregnancies in a row before fetal viability, recurrent pregnancy loss affects a fairly small yet clinically important percentage of women of reproductive age. For clinicians, it is one of the most complex

problems of reproductive medicine, occupying the crossroads of endocrinology, immunology, genetics and obstetrics [1].

The particular difficulty in managing recurrent pregnancy loss is not only due to its multifactorial character, but also because it is often not possible to identify a satisfactory cause. While abnormalities of chromosomes, structure of the uterus, endocrine disorders, autoimmune phenomena, and thrombophilia states are well-established factors, in many women, the cause of their losses remains a mystery after extensive evaluation [2]. This ongoing uncertainty often causes frustration for both patient and providers and thus reveals the extent of current limitations in the set of diagnoses.

Early pregnancy is a time of magnificent biological precision. Implantation, trophoblast invasion, placental development and immune adaptation have to occur in a finely coordinated manner. Even slight abnormalities in hormonal equilibrium, endometrial receptivity or maternal immune tolerance may interfere with this delicate process and result in pregnancy failure [3]. Increasing evidence has suggested that recurrent pregnancy loss may not be due to one pathologic event, but rather to the cumulative impact of minor dysregulations which occur in successive gestations.

Endocrine and immunological factors have been of special interest in recent years. Thyroid dysfunction, progesterone insufficiency and antiphospholipid antibodies are some of the more commonly studied conditions, as there are possible opportunities for targeted intervention [4]. Nevertheless, the presence of these abnormalities does not guarantee a loss of pregnancy, and their absence does not guarantee a successful outcome. Such variability calls for the need for personalised clinical interpretation rather than rigid categorical diagnosis.

From the clinical point of view, recurrent pregnancy loss requires a holistic and patient-centred approach. Management in modern times is not limited to identifying the etiological factors; optimisation of preconception health, structured follow-up during the early stages of pregnancy, psychological impact of repeated loss etc., are also taken into account. There are pieces of evidence to suggest that supportive care without any other initiated treatment may improve in some women, thus underscoring the importance of continuity and trust in the patient/physician relationship [5].

This study aims to elucidate the clinical features, contributing factors and pregnancy outcome of women with recurrent pregnancy loss who have been treated at a tertiary care centre in Samarkand. By conducting an analysis of real-world clinical data, the work aims to fill in the gap between theory and practice to develop a more nuanced and compassionate approach to the management of this complex condition.

Material and methods

This observational clinical study was undertaken in a tertiary-level obstetrics and gynaecology centre in Samarkand among women diagnosed with recurrent pregnancy loss. The study period was from September 2023 to September 2025, which allowed for sufficient time for structured diagnosis evaluation, longitudinal follow-up and reproductive outcome evaluation within the routine clinical setting. The design selected reflects real-life management of recurrent pregnancy loss in which clinical decisions are based on cumulative results rather than results from a single test.

A total of 89 women of reproductive age were included. Participants were recruited from both the outpatient and inpatient gynaecological services. Recurrent pregnancy loss was considered to be two or more successive spontaneous losses of pregnancy before 20 weeks of gestation. The incorporation of primary forms as well as secondary forms was included in order to capture the entire clinical spectrum. Women with a history of one sporadic miscarriage, ectopic pregnancy, molar pregnancy or elective termination were also excluded for the sake of consistency of the diagnosis.

A detailed reproductive and medical history was taken as a baseline evaluation. Particular emphasis was placed on the number and time interval between previous pregnancy losses, interpregnancy intervals, and associated obstetric problems. Medical history was focused on endocrine diseases, autoimmune diseases, thrombotic diseases and chronic systemic diseases known to affect the outcome of early pregnancy. Lifestyle factors like body mass index, smoking status and occupational stress were recorded because they could cumulatively increase reproductive risk [6].

Diagnostic assessment was conducted by a structured but individually tailored assessment protocol. Hormonal evaluation included serum thyroid-stimulating hormone, prolactin, and progesterone levels that were interpreted based on the cycle phase and gestational context. Autoimmune screening for

antiphospholipid antibodies was done in women who had clinical indications or repeated early pregnancy losses. Transvaginal ultrasonography was obtained in all participants to assess the uterine anatomy, endometrial morphology and ovarian structure. When abnormalities in the uterus were suspected, additional procedures to diagnose the condition were recommended, such as a hysteroscopy. This stepwise strategy is in agreement with current international recommendations for recurrent pregnancy loss evaluation [7].

Women who became pregnant during the period of the study were followed up prospectively. Early pregnancy monitoring was focused on confirmation of intrauterine implantation, viability of the embryo and early development of the placenta. Therapeutic interventions (progesterone supplementation, levothyroxine therapy or anticoagulant treatment) were prescribed individually, based on identified risk factors and current clinical guidelines and not as universal protocols. This individualised approach is indicative of some emerging consensus that requirements are more effectively met by individualised management than blanket treatment strategies in recurrent pregnancy loss [8].

Pregnancy outcomes were classified as early pregnancy loss, sustained pregnancy after the first trimester or live birth. Maternal complications that developed during pregnancy were registered. Data analysis had a strong focus on clinically meaningful interpretation of observed patterns rather than complex statistical modelling, to ensure that it was relevant to everyday clinical practise. All diagnostic and therapeutic procedures were conducted as part of routine care, and strict consideration was given to adherence to ethical standards and patient confidentiality [9].

Result and discussions

Evaluation of clinical records of 89 women who had experienced recurrent pregnancy loss showed that there is little uniformity and predictability to the condition. Although all the patients had a common diagnosis, their clinical course, contributory factors, and reproductive outcomes differed significantly. This variability became especially obvious when the etiological factors were analysed in relation to pregnancy outcomes, reinforcing the concept that recurrent pregnancy loss represents a spectrum of interacting mechanisms rather than a uniform disorder [10].

Endocrine abnormalities became the most common factors identified as contributing factors. Thyroid dysfunction and insufficiency of the luteal phase were frequently subtle and clinically silent, so that they became apparent only after repeated pregnancy failures. Immune - mediated and thrombophilic conditions were more frequent in women with first-trimester losses, which is suggestive of a possible involvement of impaired implantation and early placental development. Structural uterine abnormalities (less common) were usually associated with similar gestational age losses. Despite exhaustive assessment, a large proportion of women had no obvious cause for their recurrent pregnancy loss, thus demonstrating the ongoing difficulty with unexplained recurrent pregnancy loss as reported in current literature [11].

Table 1. Contributing factors identified in women with recurrent pregnancy loss (n = 89)

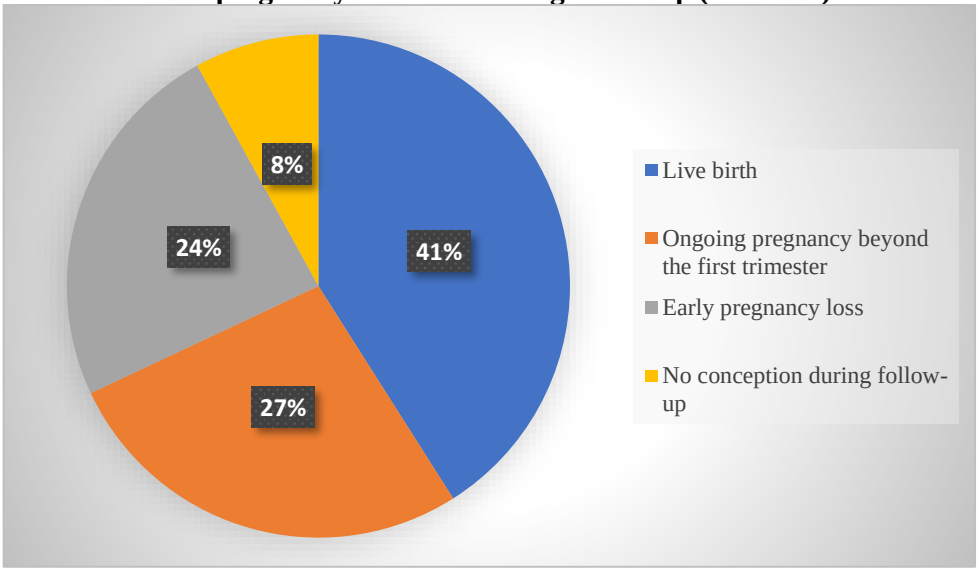
Contributing factor	Number of patients	Percentage (%)
Endocrine factors	28	31.5
Autoimmune/thrombophilic factors	19	21.3
Uterine structural abnormalities	15	16.9
Infectious or inflammatory factors	9	10.1
Unexplained	18	20.2

This table illustrates the heterogeneous etiological landscape of recurrent pregnancy loss. Endocrine and immune-related factors together accounted for more than half of the identified contributors; however, the persistent proportion of unexplained cases highlights the limitations of current diagnostic strategies. These findings are consistent with recent reports emphasising that even advanced evaluation fails to identify a definitive cause in a substantial number of patients [10].

Pregnancy outcomes observed during the follow-up period further emphasised the unpredictable nature of recurrent pregnancy loss. Some women achieved successful pregnancies following targeted intervention and close monitoring, while others experienced repeated early losses despite similar management strategies. Importantly, favourable outcomes were not limited to women with identifiable

causes, suggesting that supportive care and structured follow-up may independently influence reproductive success [12].

Figure 1. Distribution of pregnancy outcomes during follow-up (Pie chart)



The pie chart shows that almost half of the women ultimately had a live birth, which is important to show that recurrent pregnancy loss is not associated with an inability to have more children. At the same time, the persistence of early pregnancy loss in a significant proportion of patients reflects the inherent level of uncertainty of prognosis. These findings are consistent with recent evidence of high levels of outcome variability even following thorough evaluation and tailored management [11,12].

Overall, the results support the view that recurrent pregnancy loss should be considered as a dynamic clinical condition. Outcome variability observed in this cohort supports the need for individualised counselling, ongoing reassessment and flexible management strategies as opposed to deterministic expectations based only on past pregnancy history.

Discussion

The results of this study underscore the complex and heterogeneous nature of recurrent pregnancy loss and confirm knowledge in this field that this condition is not explained by a single etiological pathway. Although patients share a common clinical category, their reproductive histories, contributory factors and pregnancy outcomes show considerable variability. This observation is consistent with current views that recurrent pregnancy loss is a multifactorial disease that is influenced by the interaction of endocrine, immunological, anatomical, and environmental factors rather than being a uniform disease entity [13].

One of the most clinically-relevant observations is the preponderance of endocrine and immune-related abnormalities of affected women. Thyroid dysfunction and subtle hormonal imbalances were commonly not detected until repeated losses were experienced; thus, early screening for disturbance may not be capable of identifying clinically meaningful disturbance. These findings add to the emerging view that even mild deviations in the endocrine system may impair early placentation and embryo-maternal communication, especially in women of poor physiological reserve [14]. Importantly, the presence of such abnormalities was not a guarantee of adverse outcomes, highlighting the importance of context and cumulative risk rather than individual laboratory values.

Of special concern is the unremitting proportion of cases that could not be explained in this cohort. Despite the evaluation, a significant number of women still ended up without any obviously identifiable cause for their pregnancy loss. This is similar to data in large international studies, which report on the incidence of recurrent pregnancy loss of up to 50% for unexplained reasons. Rather than being attributed to diagnostic failure alone, such a phenomenon is presumably indicative of the involvement of mechanisms that are not yet completely understood or cannot be routinely evaluated in clinical practice,

such as subtle immune dysregulation, impaired endometrial receptivity or altered maternal-fetal signalling [15].

Pregnancy outcomes during follow-up are another way of showing the unpredictable nature of recurrent pregnancy loss. The attainment of live birth in an appreciable proportion of women, even those without identifiable etiological factors, implies that the prognosis should not be considered fixed. Supportive care, close monitoring and individualised intervention may have beneficial effects unrelated to specific treatment modalities. This observation is consistent with evidence that structured follow-up and continuity of care alone can improve reproductive outcomes, likely by reducing the stress, improving adherence, and the possibility to timely response to early pregnancy complications [16].

From a clinical perspective, these results support the importance of having a patient-centred and flexible management approach. Rather than using uniform treatment protocols, clinicians should be looking to dynamic risk assessment, repeated evaluation and individualised counselling. Equally important is addressing the psychological burden associated with recurrent pregnancy loss because emotional distress may contribute to the further exacerbation of physiologic vulnerability during early pregnancy.

Overall, the results of this study support the paradigm shift in the management of recurrent pregnancy loss. The condition should be considered not as a diagnostic determination but as a dynamic condition of reproduction demanding an approach of integrated medical, psychological and supportive medical care. Continued research to improve tools of diagnosis as well as identify novel biomarkers may further improve individualised management and ultimately improve reproductive outcomes for affected women.

Conclusion

Recurrent pregnancy loss continues to be a complex reproductive problem that goes beyond one diagnosis or one aetiology. The results of this study show that pregnancy loss in affected women is determined by a complex interaction of endocrine, immunological, anatomical and often unexplained processes. Importantly, the absence of a clearly identifiable cause is not tantamount to an unfavourable prognosis, and the presence of a certain abnormality does not necessarily predetermine failure of pregnancy. The variability in pregnancy outcome seen in recurrent pregnancy loss points to the variability of recurrent pregnancy loss. A large number of women had successful pregnancies after evaluation and individualised management, emphasising that past reproductive history should not be considered a fixed predictor of future outcomes in women. These results provide further evidence for the importance of ongoing clinical assessment, individualised intervention and realistic but optimistic counselling. From a clinical point of view, an integrated and patient-centred approach to the management of recurrent pregnancy loss is necessary. Apart from diagnostic investigations, hormonal balance, immune modulation and early pregnancy surveillance play a critical role. Equally key to this is dealing with the psychological consequences of recurrent loss, as emotional health and clinical outcomes are closely interrelated. In conclusion, recurrent pregnancy loss should be considered as a dynamic reproductive condition, rather than a deterministic diagnosis. Personalised care with structured follow-up and a multidisciplinary approach has the best potential to improve reproductive outcomes as well as patient confidence. Continued research to improve the diagnostic strategies and delve into the subtler pathophysiological mechanisms will further facilitate individualised care for women with recurrent pregnancy loss.

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