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OPTIMIZATION OF PERSONALIZED PREGRAVID PREPARATION OF WOMEN WITH MISSED MISCARRIAGE IN THE ARAL SEA REGION

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Abstract

Background: Missed miscarriage remains a highly prevalent form of early reproductive loss, representing a significant medical and social challenge. In the environmentally degraded Aral Sea region, specifically Karakalpakstan, this issue is exacerbated by severe ecological factors, endemic anemia, endocrine disruptions, and widespread micronutrient deficiencies. Standardized protocols for preconception care frequently fail to address the complex, multifactorial somatic and reproductive profiles of women residing in such regions. Objective: This study aims to develop, scientifically substantiate, and evaluate a personalized algorithm for pregravid preparation among women with a history of missed miscarriage in the Aral Sea region. Methods: A comprehensive clinical, laboratory, and anamnestic evaluation was conducted on 120 reproductive-aged women with a history of missed miscarriage. The cohort was divided into a control group receiving standard care and an intervention group receiving a region-specific, personalized pregravid preparation algorithm. Assessments included hormonal profiling, hemostasiograms, micronutrient status, and pelvic ultrasonography. Results: The regional patient profile revealed a profound incidence of extragenital pathologies, notably iron deficiency anemia, subclinical hypothyroidism, and sub-optimal vitamin D levels. The implementation of the personalized pregravid preparation algorithm led to a statistically significant improvement in somatic and reproductive health markers. Pregnancy outcomes in the intervention group demonstrated a substantial reduction in the recurrence of missed miscarriages and early pregnancy losses compared to the standard care group. Conclusion: Tailoring pregravid preparation to the specific environmental, somatic, and hemostasiological characteristics of women in ecologically unfavorable regions significantly optimizes reproductive outcomes and reduces the burden of recurrent pregnancy loss.

Keywords

Missed miscarriage, pregravid preparation, Aral Sea region, reproductive health, personalized medicine, micronutrient deficiency, early pregnancy loss.

ОПТИМИЗАЦИЯ ПЕРСОНИФИЦИРОВАННОЙ ПРЕГРАВИДАРНОЙ ПОДГОТОВКИ ЖЕНЩИН С НЕРАЗВИВАЮЩЕЙСЯ БЕРЕМЕННОСТЬЮ В РЕГИОНЕ ПРИАРАЛЬЯ

Аннотация

Введение: Неразвивающаяся беременность остается одной из наиболее частых форм ранних репродуктивных потерь. В экологически неблагополучном регионе Приаралья (Каракалпакстан) эта проблема усугубляется региональными экологическими факторами, эндемичной анемией, эндокринными нарушениями и микронутриентной недостаточностью. Стандартизированные подходы часто не учитывают этот сложный профиль. Цель: Разработать и научно обосновать персонифицированный алгоритм

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прегравидарной подготовки женщин с неразвивающейся беременностью в регионе Приаралья. Методы: Проведено комплексное клинико-лабораторное обследование 120 женщин репродуктивного возраста с неразвивающейся беременностью в анамнезе. Пациентки были разделены на группу стандартной терапии и группу персонализированного подхода. Оценивались гормональный статус, гемостазиограмма, уровень микронутриентов и данные УЗИ. Результаты: Выявлена высокая частота экстрагенитальных патологий, включая железодефицитную анемию, субклинический гипотиреоз и дефицит витамина D. Внедрение персонифицированного алгоритма привело к статистически значимому улучшению показателей соматического здоровья и снижению частоты повторных потерь беременности по сравнению с контрольной группой. Заключение: Индивидуализация прегравидарной подготовки с учетом экологических и соматических особенностей региона значительно улучшает репродуктивные исходы.

Ключевые слова

Неразвивающаяся беременность, прегравидарная подготовка, регион Приаралья, репродуктивное здоровье, персонифицированная медицина, микронутриентная недостаточность.

INTRODUCTION

Missed miscarriage, recognized as a highly prevalent and psychologically devastating form of early reproductive loss, accounts for up to twenty percent of all clinically confirmed pregnancies worldwide. Within the broader structure of first-trimester gravidar losses, the proportion of missed miscarriages reaches an alarming forty-five to sixty percent. While global obstetric practices continuously refine diagnostic and therapeutic modalities for recurrent pregnancy loss, the clinical reality in ecologically compromised regions demands a profound paradigm shift. In the specific geopolitical and geographical context of the Aral Sea region, notably the Republic of Karakalpakstan, the epidemiology of reproductive loss transcends standard medical pathology, evolving into a critical medico-social crisis. The catastrophic environmental degradation resulting from the desiccation of the Aral Sea has precipitated a cascade of adverse ecological factors, including severe water and soil salinization, agrochemical contamination, and the atmospheric dispersion of toxic particulate matter. These environmental stressors exert a relentless and cumulative toxic effect on the female reproductive system, leading to a unique regional phenotype of reproductive failure.

The population residing in this disaster zone exhibits an exceptionally high prevalence of chronic somatic dysfunctions that directly compromise gametogenesis, embryogenesis, and early placentation. Epidemiological surveillance highlights rampant iron-deficiency anemia, endemic thyroid dysfunctions primarily characterized by iodine deficiency and subclinical hypothyroidism, chronic inflammatory diseases of the pelvic organs, and pervasive macro- and micronutrient malnutrition. Standardized approaches to post-miscarriage management and subsequent preconception care, as outlined by major international reproductive medicine societies, typically assume a baseline of general environmental and somatic stability. Consequently, these unified clinical pathways frequently demonstrate reduced efficacy when applied to women in the Aral Sea region. They inherently fail to address the intricate interplay of profound chronic systemic inflammation, environmentally induced oxidative stress, subclinical coagulopathies, and subtle neuroendocrine disruptions that define the regional patient profile.

The absence of a targeted, region-specific methodology results in a high recurrence rate of missed miscarriages, contributing to a vicious cycle of physical trauma, psychological distress,

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and secondary infertility. The physiological burden of a missed miscarriage necessitates an adequate period of restoration; however, without identifying and correcting the underlying regional and individual pathological triggers, subsequent pregnancies remain at an exceptionally high risk of failure. The contemporary challenge in regional obstetrics and gynecology is therefore the transition from protocol-driven, generalized preconception care to a deeply personalized, precision-medicine approach. This approach must integrate comprehensive evaluations of the somatic, hormonal, and hemostasiological status of each woman against the backdrop of her specific environmental exposure.

Therefore, the primary objective of this scientific investigation is to develop, scientifically substantiate, and evaluate the clinical efficacy of a personalized algorithm for periconceptional and pregravid preparation specifically tailored for women with a history of missed miscarriage residing in the ecologically unfavorable conditions of Karakalpakstan. By meticulously mapping the structural causes of pregnancy loss in this demographic and defining the high-risk factors for recurrence, this research seeks to implement differentiated preventive programs that can significantly mitigate the burden of early reproductive losses and ensure positive pregnancy experiences.

MATERIALS AND METHODS

To achieve the research objectives, a comprehensive, prospective, comparative cohort study was designed and executed at the clinical facilities associated with the Medical Institute of Karakalpakstan. The study protocol was approved by the local institutional review board, and written informed consent was obtained from all participants prior to their inclusion in the clinical trial. The study population comprised one hundred and twenty reproductive-aged women who presented with a confirmed obstetric history of at least one missed miscarriage in the first trimester of pregnancy. The age of the participants ranged from eighteen to forty years, encompassing the primary demographic affected by early reproductive losses in the region.

The inclusion criteria mandated a documented history of missed miscarriage verified by ultrasonographic and histological examinations, residence in the Karakalpakstan region for a minimum of five continuous years, and a stated desire to plan a subsequent pregnancy. Exclusion criteria were strictly defined to eliminate confounding severe pathologies, including known major genetic or chromosomal anomalies in either partner, severe uncompensated extragenital diseases such as advanced heart failure or severe renal insufficiency, acute infectious diseases, and anatomical anomalies of the uterus requiring prior surgical correction.

Following initial screening and enrollment, the subjects were randomized into two distinct clinical groups to evaluate the efficacy of the proposed intervention. Group I, serving as the clinical control group, consisted of sixty women who received standard preconception counseling and preparation based on general national protocols. This standard care predominantly included basic folic acid supplementation and general lifestyle advice. Group II, the main intervention group, comprised sixty women who underwent the newly developed, deeply personalized algorithm for pregravid preparation.

The diagnostic phase for all participants was exhaustively detailed. A thorough clinical and anamnestic analysis was conducted, documenting the socio-environmental living conditions, occupational hazards, dietary habits, detailed menstrual and reproductive history, and previous gynecological interventions. The laboratory evaluation was multifaceted, designed to capture the specific physiological disruptions endemic to the region. The hormonal panel included quantitative assessments of Follicle-Stimulating Hormone, Luteinizing Hormone, Prolactin, Estradiol, Progesterone, Testosterone, Thyroid-Stimulating Hormone, and free Thyroxine,

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performed during specific phases of the menstrual cycle using enzyme-linked immunosorbent assay techniques.

Given the known association between environmental toxicity, inflammation, and thrombosis, a comprehensive coagulological investigation was prioritized. The hemostasiological status was evaluated by measuring fibrinogen levels, activated partial thromboplastin time, prothrombin index, and critical markers of intravascular coagulation such as D-dimer and lupus anticoagulant. Furthermore, recognizing the profound impact of regional malnutrition, a specialized micronutrient status assessment was conducted. This included determining serum ferritin levels as a definitive marker of iron stores, total serum calcium, magnesium, and notably, the concentration of 25-hydroxyvitamin D, reflecting the systemic vitamin D status.

Instrumental diagnostics heavily relied on high-resolution transvaginal and transabdominal ultrasonography of the pelvic organs. This imaging was utilized not only to assess structural integrity but also to evaluate endometrial receptivity, utilizing Doppler velocimetry to measure blood flow indices in the uterine and arcuate arteries during the mid-luteal phase of the cycle.

The personalized algorithm applied to Group II involved a minimum of three to six months of targeted intervention prior to conception. It mandated the rigorous correction of any identified somatic deficits. For instance, latent iron deficiency was aggressively treated with advanced liposomal or intravenous iron preparations depending on severity. Vitamin D deficiency was managed with therapeutic, dynamically monitored doses. Endocrine disruptions, particularly subclinical hypothyroidism and luteal phase defects, were managed in consultation with endocrinologists using specific targeted therapies. Furthermore, identified subclinical thrombophilias were managed with appropriate doses of low molecular weight heparins or antiplatelet agents, tailored to the individual coagulogram profile.

All collected clinical and laboratory data were subjected to rigorous statistical processing. Descriptive statistics were generated, and the normality of data distribution was tested using the Kolmogorov-Smirnov test. Continuous variables exhibiting normal distribution were compared using the Student's t-test, while non-parametric data were analyzed using the Mann-Whitney U test. Categorical variables were assessed using the Pearson Chi-square test. A probability value of less than zero point zero five was established as the threshold for statistical significance across all analyses. The statistical software package SPSS version twenty-six point zero was utilized for all computational procedures.

RESULTS

The initial comparative analysis of the clinical and anamnestic characteristics of the patients revealed a profound prevalence of somatic and gynecological morbidity, underscoring the severe impact of the regional ecological environment. The mean age of the participants did not differ significantly between the groups, standing at twenty-eight point four years. However, a detailed evaluation of their extragenital background illuminated critical vulnerabilities. Iron deficiency anemia of varying severity was diagnosed in an overwhelming majority of the cohort, affecting over seventy percent of all women. Endocrine pathologies were the second most frequent systemic disruption, with diffuse toxic goiter and autoimmune thyroiditis representing the primary clinical manifestations.

Table 1 presents the detailed baseline distribution of extragenital and gynecological morbidities among the examined women. The data vividly demonstrates that chronic inflammatory processes, particularly chronic endometritis, were universally prevalent, likely serving as a major pathophysiological substrate for the previous missed miscarriages.

Table 1: Baseline somatic and gynecological characteristics of the study population

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Clinical Characteristic	Group I (Standard Care) n=60	Group II (Personalized Care) n=60	Statistical Significance (p-value)
Iron Deficiency Anemia	43 (71.6%)	45 (75.0%)	>0.05
Thyroid Pathology	22 (36.6%)	25 (41.6%)	>0.05
Gastrointestinal Tract Diseases	18 (30.0%)	20 (33.3%)	>0.05
Chronic Pelvic Inflammatory Disease	35 (58.3%)	38 (63.3%)	>0.05
History of Chronic Endometritis	48 (80.0%)	51 (85.0%)	>0.05
Menstrual Cycle Irregularities	19 (31.6%)	21 (35.0%)	>0.05

The laboratory investigations further elucidated the systemic nature of the reproductive failures in this population. The micronutrient profiling revealed a catastrophic deficiency in Vitamin D. Less than fifteen percent of the total cohort exhibited optimal serum levels of 25-hydroxyvitamin D, with the vast majority falling into the categories of insufficiency or severe deficiency. Similarly, despite some patients exhibiting normal hemoglobin levels, serum ferritin analysis revealed a high incidence of latent iron deficiency, a condition known to severely impair cellular oxygenation and enzymatic functions critical for early embryonic development.

Table 2 details the specific hematological and biochemical parameters before the initiation of the pregravid preparation. The hemostasiogram results indicated a hypercoagulable shift in a significant subset of patients, characterized by elevated D-dimer levels and shortened activated partial thromboplastin times, suggesting an underlying state of chronic endothelial dysfunction potentially linked to environmental toxin exposure and systemic inflammation.

Table 2: Baseline laboratory and micronutrient parameters

Analyte / Parameter	Group I (Standard Care) Mean ± SD	Group II (Personalized Care) Mean ± SD	Normal Reference Range
Serum Ferritin (ng/mL)	18.4 ± 4.2	17.9 ± 3.8	30.0 - 150.0
25-hydroxyvitamin D (ng/mL)	16.2 ± 5.1	15.8 ± 4.7	30.0 - 100.0
Thyroid Stimulating Hormone (mIU/L)	3.8 ± 1.1	4.1 ± 1.3	0.4 - 4.0
D-dimer (ng/mL)	480 ± 110	510 ± 125	< 250
Fibrinogen (g/L)	4.1 ± 0.5	4.3 ± 0.6	2.0 - 4.0

Following the diagnostic phase, Group II underwent the strict, personalized pregravid preparation algorithm over a period of three to six months. This targeted approach focused on restoring the identified deficits and stabilizing chronic conditions prior to conception. Patients with iron deficiency received aggressive intravenous or highly bioavailable oral iron therapy until serum ferritin exceeded fifty nanograms per milliliter. Vitamin D was supplemented aggressively to achieve and maintain levels above forty nanograms per milliliter. Thyroid dysfunctions were meticulously managed to keep Thyroid-Stimulating Hormone strictly below two point five milli-international units per liter, the optimal threshold for conception and early pregnancy maintenance. Furthermore, women with identified hypercoagulable states received prophylactic antithrombotic therapy tailored to their specific hemostatic profiles.

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The clinical efficacy of this personalized approach became unequivocally evident when analyzing the subsequent pregnancy outcomes. The women in Group II, having undergone comprehensive physiological rehabilitation, demonstrated significantly superior reproductive metrics compared to the standard care group. The incidence of spontaneous conception within twelve months following the preparation phase was higher in the intervention group. Most importantly, the course of the subsequent pregnancies was markedly different.

Table 3 illustrates the comparative outcomes of pregnancies following the respective preparation protocols. The personalized algorithm drastically reduced the incidence of recurrent missed miscarriages. Furthermore, the frequency of placental insufficiency and fetal growth restriction, common complications linked to the regional vascular and micronutrient pathologies, was substantially mitigated in Group II.

Table 3: Comparative analysis of subsequent pregnancy outcomes

Pregnancy Outcome	**Group I (Standard Care) n=60**	**Group II (Personalized Care) n=60**	**Statistical Significance (p-value)**
Successful Conception achieved	42 (70.0%)	54 (90.0%)	<0.05
Recurrent Missed Miscarriage	11 (26.1%)	3 (5.5%)	<0.01
Spontaneous Abortion	6 (14.2%)	2 (3.7%)	<0.05
Placental Insufficiency	15 (35.7%)	6 (11.1%)	<0.01
Live Birth at Term	25 (59.5%)	49 (90.7%)	<0.001

The statistical analysis solidifies the clinical observations. The relative risk of experiencing a recurrent early pregnancy loss was radically diminished in the group that received targeted, individualized care based on their specific somatic and biochemical blueprints. The live birth rate, the ultimate metric of obstetric success, was nearly universal among the women who conceived following the personalized regional algorithm, in stark contrast to the standard care group where reproductive failures continued to exact a heavy toll.

DISCUSSION

The findings of this comprehensive study unequivocally demonstrate that the etiology of missed miscarriages in the Aral Sea region is a highly complex, multifactorial phenomenon heavily dictated by the prevailing environmental disaster. The standard epidemiological data suggesting that spontaneous fetal demise occurs in up to twenty percent of pregnancies masks the specific, concentrated severity of this issue in geographically compromised areas. Our research aligns with global observations on the psychological and physical devastation caused by recurrent pregnancy loss, but strictly contextualizes it within the unique toxicological and nutritional landscape of Karakalpakstan.

International guidelines, including those formulated by the European Society of Human Reproduction and Embryology and the American College of Obstetricians and Gynecologists, provide excellent foundational protocols for managing early pregnancy loss. However, these documents inherently rely on generalized population data. Our clinical analysis reveals that applying uniform, standardized pregravid preparation pathways to women in Karakalpakstan fails to address the foundational causes of their reproductive failure. The extremely high prevalence of profound iron deficiency, latent thyroid dysfunction, and critical Vitamin D

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depletion identified in our cohort acts as a powerful, combined teratogenic and abortifacient force. When the maternal organism is chronically deprived of elemental physiological building blocks due to regional dietary and environmental factors, normal placentation and embryonic organogenesis are severely compromised, leading inevitably to embryonic arrest.

The implementation of the personalized periconceptional preparation algorithm fundamentally altered the reproductive trajectory of the intervention group. By shifting the clinical focus from reactive management of the miscarriage to proactive, aggressive correction of subclinical systemic pathologies prior to conception, we observed a dramatic reduction in recurrent losses. The normalization of serum ferritin, for example, is not merely a correction of a laboratory value; it ensures adequate oxygen transport to the developing trophoblast, preventing the oxidative stress-induced apoptosis that characterizes many missed miscarriages. Similarly, the meticulous management of thyroid function and Vitamin D levels modulates the immune response at the maternal-fetal interface, preventing immunological rejection of the conceptus.

Furthermore, our study highlights the critical role of hemostasiological assessment. The environmentally induced state of chronic, low-grade inflammation evident in the region frequently translates into endothelial dysfunction and a pro-thrombotic state. By identifying and individually managing these micro-coagulopathies before conception, we successfully prevented the microthrombosis in the chorionic villi that is a well-documented mechanism of early fetal demise. The statistically significant decrease in placental insufficiency and subsequent high live birth rate in the personalized care group serves as irrefutable evidence that optimizing the maternal physiological environment is paramount.

The scientific novelty of this research lies in its specific regional orientation. It proves that personalized medicine in obstetrics cannot rely solely on genetic or highly advanced molecular screening; in ecologically disadvantaged regions, precision medicine must first and foremost address the severe, environmentally driven metabolic and somatic dysfunctions. The practical significance is immediate and profound: integrating this comprehensive, diagnostically driven algorithm into routine regional clinical practice can drastically reduce maternal morbidity, decrease the psychological trauma associated with recurrent reproductive failure, and significantly improve demographic indicators in the Aral Sea region.

CONCLUSION

In conclusion, the problem of missed miscarriage in the ecologically unfavorable conditions of Karakalpakstan is characterized by a high frequency and a complex etiology rooted in regional somatic and biochemical dysfunctions. The traditional, unified approaches to preconception care are clinically insufficient to overcome the compounding effects of endemic anemia, endocrine disruptions, and severe micronutrient deficiencies. The development and implementation of a personalized, regionally oriented algorithm for pregravid preparation, which mandates the meticulous diagnosis and correction of individual somatic, hormonal, and hemostasiological statuses prior to conception, proved highly effective. This individualized strategy resulted in a statistically significant reduction in the incidence of recurrent missed miscarriages, minimized the occurrence of placental complications, and drastically increased the rate of successful live term births. Therefore, the wide-scale integration of differentiated, personalized preventive and preparatory programs into the regional healthcare system is a scientifically justified and clinically urgent necessity to protect and optimize the reproductive health of women in the Aral Sea region.

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