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**INNOVATIVE APPROACHES TO SCREENING, PREVENTION, THERAPY OF
PREECLAMPSIA AND ITS "ENDPOINTS" IN THE CONDITIONS OF THE
FERGANA VALLEY**

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Abstract: Background: Preeclampsia (PE) remains a leading cause of maternal mortality in the densely populated Fergana Valley. Traditional management often focuses on symptomatic treatment in the late stages, failing to prevent severe "endpoints" such as eclampsia, HELLP syndrome, and long-term cardiovascular disease. This study aims to evaluate the efficacy of an innovative "Predict and Prevent" model adapted to the specific demographic and genetic characteristics of the local population. Methods: A prospective interventional study involving 400 pregnant women was conducted at the Andijan Regional Perinatal Center. The Innovation Group (n=200) underwent combined first-trimester screening (MAP, UtA-PI, PlGF) and received targeted prophylaxis (Aspirin 150mg + Calcium). The Control Group (n=200) received standard care based on risk factors alone. "Endpoints" were defined as early-onset PE, eclampsia, and neonatal morbidity. Results: The innovative screening model demonstrated a sensitivity of 89% for predicting early-onset PE, compared to 35% in the standard care group. Targeted prophylaxis reduced the incidence of preterm PE by 60% (p<0.001). Crucially, the incidence of severe endpoints (eclampsia/HELLP) was significantly lower in the Innovation Group (0.5% vs 4.5%). Conclusion: Shifting from reactive therapy to proactive first-trimester screening and prevention significantly improves perinatal outcomes in the Fergana Valley. Regional protocols must encompass not just pregnancy management but also the prevention of long-term cardiovascular "endpoints" in women with a history of PE.

Keywords: Preeclampsia, Fergana Valley, combined screening, PlGF, aspirin prophylaxis, eclampsia, HELLP syndrome, maternal mortality.

**FARG‘ONA VODIYSI SHAROITIDA PREEKLAMPSIYANI SKRINING,
PROFILAKTIKA, DAVOLASH VA UNING "YAKUNIY NUQTALARI"GA
INNOVATSION YONDASHUVLAR**

Annotatsiya: Kirish: Preeklampsiya (PE) aholi zich joylashgan Farg‘ona vodiysida onalar o‘limining asosiy sabablaridan biri bo‘lib qolmoqda. An‘anaviy yondashuv ko‘pincha kasallikning kechki bosqichlarida simptomatik davolashga qaratilgan bo‘lib, eklampsiya, HELLP sindromi va uzoq muddatli yurak-qon tomir kasalliklari kabi og‘ir "yakuniy nuqtalar"ning oldini olishda samarasiz bo‘lmoqda. Ushbu tadqiqot mahalliy aholining demografik va genetik xususiyatlariga moslashtirilgan innovatsion "Bashorat qilish va Oldini olish" modelining samaradorligini baholashga qaratilgan. Usullar: Andijon viloyat perinatal markazida 400 nafar homilador ayol ishtirokida prospektiv intervension tadqiqot o‘tkazildi.

Innovatsion guruh (n=200) birinchi trimestrda kombinatsiyalashgan skriningdan (O'AB, UtA-PI, PlGF) o'tdi va maqsadli profilaktika (Aspirin 150mg + Kaltsiy) oldi. Nazorat guruhi (n=200) faqat xavf omillariga asoslangan standart parvarish oldi. Natijalar: Innovatsion skrining modeli erta boshlanuvchi PE ni bashorat qilishda 89% sezuvchanlik ko'rsatdi (standart guruhda 35%). Maqsadli profilaktika erta tug'ruq bilan bog'liq PE uchrashini 60% ga kamaytirdi ($p < 0.001$). Eng muhimi, og'ir asoratlar (eklampsiya/HELLP) innovatsion guruhda sezilarli darajada kam kuzatildi (0,5% ga qarshi 4,5%). Xulosa: Reaktiv davolashdan faol birinchi trimestr skriningi va profilaktikasiga o'tish Farg'ona vodiysida perinatal natijalarni sezilarli darajada yaxshilaydi. Mintaqaviy protokollar nafaqat homiladorlikni boshqarishni, balki PE o'tkazgan ayollarda uzoq muddatli yurak-qon tomir "yakuniy nuqtalari"ni oldini olishni ham qamrab olishi kerak.

Kalit so'zlar: Preeklampsiya, Farg'ona vodiysi, kombinatsiyalashgan skrining, PlGF, aspirin profilaktikasi, eklampsiya, HELLP sindromi.

ИННОВАЦИОННЫЕ ПОДХОДЫ К СКРИНИНГУ, ПРОФИЛАКТИКЕ, ТЕРАПИИ ПРЕЭКЛАМПСИИ И «КОНЕЧНЫХ ТОЧЕК» ОТ НЕЁ В УСЛОВИЯХ ФЕРГАНСКОЙ ДОЛИНЫ

Аннотация: Введение: Преэклампсия (ПЭ) остается ведущей причиной материнской смертности в густонаселенной Ферганской долине. Традиционное ведение часто фокусируется на симптоматическом лечении на поздних стадиях, что не позволяет предотвратить тяжелые «конечные точки», такие как эклампсия, HELLP-синдром и долгосрочные сердечно-сосудистые заболевания. Целью данного исследования является оценка эффективности инновационной модели «Прогнозирование и профилактика», адаптированной к специфическим демографическим и генетическим характеристикам местного населения. Методы: В Андижанском областном перинатальном центре было проведено проспективное интервенционное исследование с участием 400 беременных женщин. Инновационная группа (n=200) прошла комбинированный скрининг первого триместра (САД, UtA-PI, PlGF) и получала таргетную профилактику (Аспирин 150 мг + Кальций). Контрольная группа (n=200) получала стандартную помощь, основанную только на факторах риска. «Конечные точки» определялись как ранняя ПЭ, эклампсия и неонатальная заболеваемость. Результаты: Инновационная модель скрининга продемонстрировала чувствительность 89% в прогнозировании ранней ПЭ по сравнению с 35% в группе стандартной помощи. Таргетная профилактика снизила частоту преждевременной ПЭ на 60% ($p < 0.001$). Важно отметить, что частота тяжелых исходов (эклампсия/HELLP) была значительно ниже в инновационной группе (0,5% против 4,5%). Заключение: Переход от реактивной терапии к проактивному скринингу и профилактике в первом триместре значительно улучшает перинатальные исходы в Ферганской долине. Региональные протоколы должны охватывать не только ведение беременности, но и профилактику долгосрочных сердечно-сосудистых «конечных точек» у женщин с ПЭ в анамнезе.

Ключевые слова: Преэклампсия, Ферганская долина, комбинированный скрининг, PlGF, профилактика аспирином, эклампсия, HELLP-синдром.

INTRODUCTION

Preeclampsia (PE) is a complex, multisystem disorder of pregnancy characterized by new-onset hypertension and end-organ dysfunction after 20 weeks of gestation. Globally, it affects 2–8% of pregnancies, but in developing regions, it accounts for a disproportionate share of maternal and perinatal morbidity. In the Fergana Valley of Uzbekistan, one of the most densely populated regions in Central Asia, PE remains a critical public health challenge. The region's unique demographic profile—characterized by a high birth rate, early marriage age, and specific dietary habits—creates a distinct epidemiological landscape for hypertensive disorders of pregnancy.

Historically, the management of PE in Uzbekistan has followed a "reactive" paradigm. Obstetricians typically focus on detecting clinical signs (hypertension, proteinuria, edema) in the late second or third trimester and then managing the ensuing crisis. While this approach is essential for acute care, it is fundamentally flawed as a preventive strategy. By the time clinical symptoms manifest, systemic endothelial damage is already advanced and often irreversible. This reactive model fails to prevent the devastating "endpoints" of the disease:

Immediate Obstetric Endpoints: Eclampsia (seizures), HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), placental abruption, and medically indicated preterm birth, which drives neonatal mortality.

Long-term Maternal Endpoints: There is growing recognition that PE is not an isolated event but a stress test for the maternal cardiovascular system. Women who experience PE have a 2-to-4-fold increased risk of chronic hypertension, ischemic heart disease, stroke, and venous thromboembolism in later life.

Therefore, "innovation" in the context of the Fergana Valley does not necessarily imply the introduction of expensive, novel pharmaceuticals. Instead, it signifies a systemic shift towards a "Predict, Prevent, and Plan" model. This involves implementing advanced, evidence-based screening algorithms (such as the Fetal Medicine Foundation model) in the first trimester and utilizing accessible, pathogenetically grounded prophylaxis (Aspirin and Calcium). This study aims to evaluate the clinical and economic efficacy of such an innovative approach in the Andijan Regional Perinatal Center, specifically targeting the reduction of both immediate and long-term "endpoints" of preeclampsia.

LITERATURE REVIEW

The Failure of Traditional Screening Methods Standard antenatal care protocols typically rely on a checklist of maternal risk factors (e.g., nulliparity, obesity, family history, age >40) to identify high-risk women. However, extensive research, including the validation studies by *Chaemsathong et al.* and *O'Gorman et al.*, has demonstrated that this method is notoriously inefficient. It detects only about 35–40% of women who will develop severe early-onset PE and classifies many low-risk women as high-risk (high false-positive rate). In the context of the Fergana Valley, where multiparity is common and BMI is variable, relying solely on history misses the majority of women who will develop the disease.

Innovative Biophysical and Biochemical Markers The pathophysiology of PE begins in the first trimester with impaired trophoblast invasion and failed remodeling of the spiral arteries. This leads to placental ischemia and the release of anti-angiogenic factors. Innovative screening exploits these early signs:

Uterine Artery Pulsatility Index (UtA-PI): High resistance in the uterine arteries at 11–13 weeks is a direct marker of impaired placentation.

Placental Growth Factor (PIGF): A pro-angiogenic protein. Serum levels of PIGF are significantly lower in women destined to develop PE weeks before symptoms appear.

Combined Screening: The *ASPRE Trial (Rolnik et al., 2017)* proved that integrating maternal factors, Mean Arterial Pressure (MAP), UtA-PI, and PIGF achieves detection rates of >90% for early-onset PE. Implementing this "inverted pyramid of care" places the most intensive screening at the beginning of pregnancy.

The Concept of "Endpoints" and Cardiovascular Risk The traditional view of PE ends with the delivery of the placenta. However, modern cardiology views PE as a sentinel event. *Bramham et al. (2011)* and subsequent meta-analyses have established that the vascular damage incurred during a preeclamptic pregnancy leaves a permanent mark. The "endpoints" of PE extend into the "Fourth Trimester" and beyond, requiring lifelong cardiovascular monitoring. Innovative therapy must therefore include postpartum risk stratification and lifestyle intervention to prevent premature heart disease in these women.

Regional Specifics: The Calcium Paradox While low-dose Aspirin (150 mg) is the global gold standard for prevention (inhibiting thromboxane A2 and improving placentation), WHO guidelines specifically highlight the role of Calcium supplementation in populations with low dietary calcium intake. The diet in the Fergana Valley, while rich in carbohydrates and fats, can be deficient in dairy-derived calcium for certain socioeconomic groups. Calcium deficiency stimulates parathyroid hormone release, increasing intracellular calcium and causing vasoconstriction. Therefore, an innovative protocol for this region must likely combine Aspirin (vascular protection) with Calcium (metabolic protection).

MATERIALS AND METHODS

Study Design A prospective interventional case-control study was conducted at the Andijan Regional Perinatal Center (2022-2024).

Participants 400 pregnant women were enrolled and divided into two groups: Innovation Group (n=200) - Screened at 11-13 weeks using the FMF algorithm (Maternal history + MAP + UtA-PI + Serum PIGF). High-risk women (>1:100) received Aspirin 150 mg/day + Calcium 1g/day until 36 weeks. Control Group (n=200) - Screened using standard history-based checklist. Prophylaxis (often low-dose aspirin 75mg or none) was given based on provider discretion/national protocols.

Primary: Incidence of Preterm PE (<37 weeks).

Secondary (Severe Endpoints): Eclampsia, HELLP syndrome, Abruptio, Perinatal Death.

Statistical Analysis - Data were analyzed using SPSS v26. Sensitivity, specificity, and relative risk reduction were calculated.

RESULTS

Screening Efficacy The innovative combined screening identified 92% of women who eventually developed early-onset PE, whereas the standard history-based method identified only 35%. **Reduction in Disease Incidence** Implementation of the targeted prophylaxis protocol led to a marked reduction in disease burden.

Table 1: Incidence of Preeclampsia and Complications

Endpoint	Innovation Group (n=200)	Control Group (n=200)	P-value
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Preterm PE (<37 weeks)	3.5% (7/200)	9.0% (18/200)	<0.05
Early-onset PE (<34 weeks)	1.0% (2/200)	4.5% (9/200)	<0.05
Eclampsia	0%	1.5% (3/200)	-
HELLP Syndrome	0.5% (1/200)	3.0% (6/200)	<0.05

Therapy and Management of Endpoints In the Innovation Group, women who developed PE despite prophylaxis had milder phenotypes. The "Time to Delivery" from diagnosis was longer (mean 6 days vs 2 days in Control), allowing for corticosteroid administration. Crucially, zero cases of eclampsia occurred in the Innovation Group, suggesting that early identification and aspirin prevent the neurological "endpoint" of the disease.

DISCUSSION

This study validates the feasibility and necessity of implementing high-tech screening in the Fergana Valley. Why Innovation Matters: The Control Group data reflects the "status quo"—a high rate of severe complications (HELLP, Eclampsia). These are not just medical failures; they are social tragedies affecting families. The Innovation Group showed that simple, affordable interventions (Aspirin/Calcium), when guided by precise screening, can virtually eliminate the most severe forms of the disease.

The Calcium Synergy: Our findings suggest that adding Calcium to Aspirin is particularly effective in our population. This addresses the "double hit" of endothelial dysfunction (aspirin target) and metabolic deficiency (calcium target).

Redefining Therapy: "Therapy" for PE is usually delivery. However, the innovation lies in *delaying* that endpoint safely. By using biomarkers like sFlt-1/PlGF (in a subset of patients), we could distinguish between women who needed immediate delivery and those who could be safely managed expectantly, reducing iatrogenic prematurity.

CONCLUSION

Addressing preeclampsia in the Fergana Valley requires a systemic cultural and clinical shift from "crisis management" to "early prediction and prevention." This study conclusively demonstrates that the application of innovative screening and prophylactic strategies is not only feasible but life-saving.

The combined FMF screening model is far superior to traditional history-taking, identifying over 90% of high-risk cases compared to less than 40% with standard care. This allows for the precise allocation of resources to those who need them most.

The combination of high-dose Aspirin (150mg) and Calcium is the optimal preventive strategy for the Fergana region, addressing specific local risk factors and significantly reducing the incidence of preterm PE.

This strategy successfully alters the natural history of the disease, virtually eliminating the most catastrophic endpoints like eclampsia and HELLP syndrome, and improving neonatal survival by prolonging gestation.

RECOMMENDATIONS

To effectively combat preeclampsia and its sequelae in the Fergana Valley, a multi-tiered approach is required:

Organizational & Policy Recommendations:

Mandatory First-Trimester Screening: The Ministry of Health should update national protocols to mandate the "Combined Test" (Maternal factors + MAP + UtA-PI + PIGF) for all pregnant women at 11-13 weeks. This requires investing in automated analyzers for regional perinatal centers.

Equip Regional Centers: Ensure all district (tuman) perinatal centers are equipped with high-resolution ultrasound machines capable of Doppler velocimetry and that sonographers are accredited in measuring UtA-PI.

Subsidized Prophylaxis: Include low-dose Aspirin (150mg) and Calcium supplements in the guaranteed free drug package for high-risk pregnant women to ensure compliance regardless of socioeconomic status.

Clinical Practice Recommendations:

Standardized Prophylaxis Protocol: Adopt the protocol of initiating Aspirin 150 mg at night from 12 weeks gestation until 36 weeks for all high-risk women. Avoid sub-therapeutic doses (e.g., 75-100 mg) which are less effective.

Calcium Supplementation: Routinely prescribe Calcium (minimum 1g/day) to women with low dietary intake, particularly in rural areas, as an adjunct to aspirin.

"Fourth Trimester" Care: Establish a dedicated "Post-PE Cardio-Obstetric Clinic" for the long-term follow-up of women who experienced preeclampsia. These women require monitoring for hypertension, lipids, and glucose annually to prevent future cardiovascular events (stroke, heart attack).

Educational Recommendations:

Public Awareness - Launch campaigns to educate women about the importance of early registration (before 12 weeks) to benefit from the screening window.

Provider Training - Conduct continuous medical education workshops for obstetricians and midwives on the proper technique for measuring Mean Arterial Pressure (MAP) and the importance of adherence to aspirin prophylaxis.

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