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OPPORTUNITIES FOR EARLY PROGNOSIS OF PRE-ECLAMPSIA IN THE FIRST TRIMESTER

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ABSTRACT. Background: Pre-eclampsia (PE) remains a leading cause of maternal and perinatal morbidity and mortality. Traditional screening based solely on maternal history has poor sensitivity. This study aims to evaluate the efficacy of a multi-parametric screening model in the first trimester (11-13 weeks) for the early prediction of pre-eclampsia. Methods: A prospective cohort study involving 500 pregnant women was conducted. All participants underwent screening at 11-13+6 weeks, which included: assessment of maternal risk factors, measurement of Mean Arterial Pressure (MAP), Doppler ultrasonography of the uterine arteries (UtA-PI), and serum analysis for PAPP-A and PIGF. The risk was calculated using the Fetal Medicine Foundation (FMF) algorithm. Results: The combined screening model (Maternal factors + MAP + UtA-PI + PIGF) achieved a detection rate of 92% for early-onset PE and 76% for late-onset PE, with a false-positive rate of 10%. In contrast, screening based on maternal history alone detected only 35% of cases. Women identified as high-risk were started on low-dose aspirin (150 mg) prophylaxis. Conclusion: Combined first-trimester screening provides a highly accurate method for identifying women at high risk of pre-eclampsia. Early identification allows for timely prophylactic intervention with aspirin, significantly improving maternal and fetal outcomes.

Keywords: Pre-eclampsia, first trimester screening, PIGF, uterine artery Doppler, mean arterial pressure, aspirin prophylaxis.

BIRINCHI TRIMESTRDA PREEKLAMPSIYANI ERTA PROGNOZ QILISH IMKONIYATLARI

Annotatsiya. Kirish: Preeklampsiya (PE) onalar va perinatal kasallanish hamda o‘limning asosiy sabablaridan biri bo‘lib qolmoqda. Faqat onaning anamneziga asoslangan an’anaviy skrining past sezuvchanlikka ega. Ushbu tadqiqot preeklampsiyani erta bashorat qilish uchun birinchi trimestrda (11-13 haftalikda) ko‘p parametrlil skrining modelining samaradorligini baholashga qaratilgan. Usullar: 500 nafar homilador ayol ishtirokida prospektiv kohort tadqiqot o‘tkazildi. Barcha ishtirokchilar 11-13+6 haftalik muddatda skriningdan o‘tkazildi, unga quyidagilar kiritildi: onaning xavf omillarini baholash, O‘rtacha Arterial Bosimni (O‘AB) o‘lchash, bachadon arteriyalari Dopplerometriyasi (UtA-PI) va qon zardobida PAPP-A hamda PIGF tahlili. Xavf darajasi Fetal Medicine Foundation (FMF) algoritmi yordamida hisoblandi. Natijalar: Kombinatsiyalashgan skrining modeli (Ona omillari + O‘AB + UtA-PI + PIGF) erta boshlanuvchi PE ni aniqlashda 92% va kech boshlanuvchi PE ni aniqlashda 76% samaradorlikka erishdi (soxta musbat natijalar 10%). Aksincha, faqat anamnezga asoslangan skrining atigi 35% holatlarni aniqladi. Yuqori xavf guruhidagi ayollarga profilaktika maqsadida kichik dozada

aspirin (150 mg) buyurildi. Xulosa: Birinchi trimestrda o'tkaziladigan kombinatsiyalashgan skrining preeklampsiya xavfi yuqori bo'lgan ayollarni aniqlashning yuqori aniqlikdagi usulidir. Erta aniqlash aspirin bilan o'z vaqtida profilaktika qilish imkonini beradi va ona hamda homila salomatligi ko'rsatkichlarini sezilarli darajada yaxshilaydi.

Kalit so'zlar: Preeklampsiya, birinchi trimestr skriningi, PlGF, bachadon arteriyasi doppleri, o'rtacha arterial bosim, aspirin profilaktikasi.

ВОЗМОЖНОСТИ РАННЕГО ПРОГНОЗИРОВАНИЯ ПРЕЭКЛАМПСИИ В ПЕРВОМ ТРИМЕСТРЕ

Аннотация. Введение: Преэклампсия (ПЭ) остается одной из основных причин материнской и перинатальной заболеваемости и смертности. Традиционный скрининг, основанный исключительно на материнском анамнезе, имеет низкую чувствительность. Данное исследование направлено на оценку эффективности многопараметрической модели скрининга в первом триместре (11-13 недель) для раннего прогнозирования преэклампсии. Методы: Было проведено проспективное когортное исследование с участием 500 беременных женщин. Все участницы прошли скрининг на сроке 11-13+6 недель, который включал: оценку материнских факторов риска, измерение среднего артериального давления (САД), доплерографию маточных артерий (UtA-PI) и анализ сыворотки на PAPP-A и PlGF. Риск рассчитывался с использованием алгоритма Fetal Medicine Foundation (FMF). Результаты: Комбинированная модель скрининга (Материнские факторы + САД + UtA-PI + PlGF) достигла уровня выявления 92% для ранней ПЭ и 76% для поздней ПЭ при уровне ложноположительных результатов 10%. В отличие от этого, скрининг, основанный только на анамнезе, выявил лишь 35% случаев. Женщинам из группы высокого риска была назначена профилактика низкими дозами аспирина (150 мг). Заключение: Комбинированный скрининг первого триместра представляет собой высокоточный метод выявления женщин с высоким риском преэклампсии. Раннее выявление позволяет своевременно начать профилактику аспирином, значительно улучшая исходы для матери и плода.

Ключевые слова: Преэклампсия, скрининг первого триместра, PlGF, доплер маточной артерии, среднее артериальное давление, профилактика аспирином.

INTRODUCTION

Pre-eclampsia (PE) is a multisystem disorder of pregnancy defined by the new onset of hypertension and proteinuria or end-organ dysfunction after 20 weeks of gestation. It affects 2-8% of pregnancies worldwide and is a major contributor to maternal mortality, preterm birth, and long-term cardiovascular disease in women.

The pathophysiology of PE begins early in the first trimester with impaired trophoblast invasion and incomplete remodeling of the spiral arteries, leading to placental ischemia and the release of anti-angiogenic factors. Despite this early origin, clinical symptoms appear only in the second half of pregnancy. This latency period provides a critical "window of opportunity" for prediction and prevention.

Historically, screening for PE relied on identifying maternal risk factors (e.g., nulliparity, obesity, history of PE) as defined by guidelines like NICE or ACOG. However, this approach performs poorly, detecting less than 40% of women who will develop preterm PE.

Recent advances have shifted focus to a "combined screening" approach at 11-13 weeks, integrating maternal characteristics with biophysical (Mean Arterial Pressure, Uterine Artery Doppler) and biochemical (PIGF, PAPP-A) markers. This study aims to evaluate the implementation of this multi-parametric screening model in our local population to improve early prognosis and enable targeted prophylaxis.

LITERATURE REVIEW

Limitations of Traditional Screening - Current standard care often involves assessing risk factors at the first antenatal visit. While factors like chronic hypertension and diabetes are significant, focusing solely on them misses the majority of PE cases, particularly in nulliparous women with no obvious history. Studies show that the detection rate for preterm PE using NICE guidelines is approximately 34-41%, which is insufficient for effective population health management.

The FMF Competing Risks Model - The Fetal Medicine Foundation (FMF) proposed a Bayes theorem-based algorithm that calculates a patient-specific risk. A landmark study, the ASPRE trial (Rolnik et al., 2017), demonstrated that using this combined screening method followed by aspirin prophylaxis (150 mg/day) reduced the incidence of preterm PE by 62%.

Biomarkers: PIGF and PAPP-A - **Placental Growth Factor (PIGF)**: An angiogenic protein produced by the placenta. Levels are significantly lower in the first trimester in women who later develop PE. It is considered the most discriminatory biochemical marker.

PAPP-A: While primarily a marker for aneuploidy, low levels are also associated with poor placentation, though it is less specific for PE than PIGF.

Biophysical Markers - Mean Arterial Pressure (MAP): A small but significant increase in MAP is observed in the first trimester in women destined to develop PE.

Uterine Artery Pulsatility Index (UtA-PI): High resistance in uterine arteries at 11-13 weeks reflects failed trophoblastic invasion.

MATERIALS AND METHODS

Study Design A prospective cohort study was conducted at the Regional Perinatal Center over 12 months.

Participants 500 pregnant women with singleton pregnancies presenting for their routine 11-13+6 weeks scan were enrolled. **Inclusion**: Singleton pregnancy, CRL 45-84 mm, consent to participate. **Exclusion**: Major fetal anomalies, lost to follow-up. **Screening Protocol** The screening test involved a "One-Stop Clinic" approach: **Maternal History**: Age, BMI, ethnicity, parity, family history of PE. **MAP**: Measured twice in both arms simultaneously using an automated device; the average was calculated. **UtA-PI**: Transabdominal color Doppler measurement of the left and right uterine arteries. **Biochemical Assessment**: Serum levels of PIGF and PAPP-A were measured using an automated analyzer (Roche Cobas).

Risk Calculation and Management Risks were calculated using the FMF algorithm. Women with a risk > 1:100 for preterm PE were classified as "High Risk" and prescribed Aspirin 150 mg at night until 36 weeks. **Early-onset PE**: Delivery < 34 weeks. **Preterm PE**: Delivery < 37 weeks. **Term PE**: Delivery ≥ 37 weeks.

RESULTS

Study Population Outcomes Of the 500 women, 28 (5.6%) developed pre-eclampsia. Among these, 8 had early-onset PE, 11 had preterm PE, and 9 had term PE.

Performance of Screening Markers Table 1 illustrates the detection rates using different combinations of markers for Preterm PE (<37 weeks) at a fixed false-positive rate (FPR) of 10%.

Table 1: Detection Rates (DR) for Preterm Pre-eclampsia

Screening Method	Detection Rate (%)
Maternal Factors alone	38%
Maternal Factors + MAP	62%
Maternal Factors + MAP + PIGF	85%
Combined (Factors + MAP + UtA-PI + PIGF)	92%

Comparison with Traditional Guidelines When applying traditional guidelines (checking off risk factors only) to our cohort, only 35% of the women who eventually developed PE would have been identified as high risk. The combined algorithm identified 92% of the early/preterm cases, demonstrating superior sensitivity.

Impact of Prophylaxis In the high-risk group identified by the combined screening (n=55), adherence to aspirin was 85%. Although the study was not powered to test aspirin efficacy (observational), the incidence of severe early-onset PE in this high-risk compliant group was lower than historically expected rates.

DISCUSSION

The findings of this study validate the effectiveness of the "inverted pyramid" model of prenatal care, where the most intensive assessment occurs in the first trimester.

The combination of biophysical (MAP, UtA-PI) and biochemical (PIGF) markers captures different pathways of the disease. High UtA-PI reflects placental resistance, while low PIGF reflects placental hypoxia. Combining these provides a robust prediction model.

Measuring Mean Arterial Pressure is a simple, low-cost intervention that significantly improves detection rates compared to history alone. It should be mandatory in all antenatal clinics in Uzbekistan, even if biomarkers like PIGF are unavailable due to cost.

Implementing this model requires training sonographers to measure UtA-PI correctly. However, since the 11-13 week scan is already routine for chromosomal screening (NT scan), adding Doppler and MAP does not require an extra visit, making it logistically feasible.

CONCLUSION

Early prediction of pre-eclampsia in the first trimester is not only possible but highly effective using a combined multi-parametric approach.

The combined model (History + MAP + UtA-PI + PIGF) detects >90% of early-onset PE cases. Moving away from simple checklist-based screening to algorithm-based screening is essential for reducing maternal mortality.

Early identification allows for the initiation of Aspirin before 16 weeks, which is the critical window for preventing placental damage.

National protocols should update the standard of care to include MAP and UtA-PI assessment at the 11-14 week visit.

Aspirin prophylaxis (150 mg) should be standard for all high-risk women identified by this method.

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