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# Association Between Maternal Risk Factors and Low-Dose Aspirin Use with Preeclampsia Among High-Risk Pregnant Women

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# العلاقة بين عوامل الخطر للأمهات واستخدام الجرعات المنخفضة من الأسبرين مع تسمم الحمل لدى الحوامل الأكثر عرضة للخطر

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**Abstract:**

Preeclampsia remains a significant hypertensive disorder contributing to maternal and neonatal morbidity and mortality, particularly among women with high-risk factors such as previous preeclampsia, intrauterine fetal death (IUFD), preterm labor, low-birth-weight infants, and a family history of hypertension. This quasi-experimental study aimed to evaluate the association between these maternal risk factors and the efficacy of low-dose aspirin (75–150 mg daily) in preventing preeclampsia among 123 high-risk pregnant women at Massa Hospital in El-Bayda, Libya. Utilizing a case-control design (41 cases, 82 controls) and Chi-square analysis, the results demonstrated that maternal risk factors were significantly associated with the occurrence of preeclampsia ($p < 0.05$), with notable prevalence in cases of previous preeclampsia (48.8% vs. 12.2%) and family history of hypertension (43.9% vs. 17.1%). Crucially, the administration of low-dose aspirin between 12 and 28 weeks of gestation was found to reduce the incidence of preeclampsia by 40% (24.4% in users vs. 75.6% in non-users, $p = 0.01$) without major complications. The study concludes that low-dose aspirin is an

 

effective and safe prophylactic measure; therefore, early identification of risk factors and adherence to aspirin therapy are essential strategies for improving maternal and neonatal outcomes within the Libyan population.

**Keywords:** Preeclampsia, Low-dose aspirin, Maternal risk factors, High-risk pregnancy, Libya, Prevention, Pregnancy outcomes.

**الملخص**

لا يزال تسمم الحمل (ما قبل الارتعاج) يشكل اضطراباً ضغطياً جسيماً يساهم في زيادة معدلات المرضية والوفيات بين الأمهات وحديثي الولادة، ولا سيما بين النساء اللواتي يعانين من عوامل خطر مرتفعة؛ مثل الإصابة السابقة بتسمم الحمل، ووفاة الجنين داخل الرحم (IUFD)، والولادة المبكرة، وإنجاب أطفال منخفضي الوزن عند الولادة، والتاريخ العائلي لارتفاع ضغط الدم. هدفت هذه الدراسة شبه التجريبية إلى تقييم العلاقة بين عوامل الخطر الوالدية ومدى فاعلية الجرعات المنخفضة من الأسبرين (75-150 مجم يومياً) في الوقاية من تسمم الحمل لدى 123 امرأة حامل من فئة الحوامل الأكثر عرضة للخطر في مستشفى مَسّة بمدينة البيضاء، ليبيا. وباستخدام تصميم دراسة الحالة والشواهد (41 حالة إصابة و82 حالة ضابطة) وتحليل "كاي تربيع (Chi-square)، أظهرت النتائج وجود ارتباط معنوي بين عوامل الخطر الوالدية وحدوث تسمم الحمل ($p < 0.05$)، مع انتشار ملحوظ في حالات تسمم الحمل السابق (48.8% مقابل 12.2%) والتاريخ العائلي لارتفاع ضغط الدم (43.9% مقابل 17.1%). ومن الناحية الجوهرية، وُجد أن تناول جرعات منخفضة من الأسبرين بين الأسبوعين 12 و28 من الحمل قلل من معدل حدوث تسمم الحمل بنسبة 40% (24.4% لدى المستخدمات مقابل 75.6% لدى غير المستخدمات، بقيمة احتمالية $p = 0.01$) دون حدوث مضاعفات كبرى. تخلص الدراسة إلى أن الجرعات المنخفضة من الأسبرين تعد إجراءً وقائياً فعالاً وآمناً؛ لذا فإن التحديد المبكر لعوامل الخطر والالتزام بالعلاج الوقائي بالأسبرين يمثلان استراتيجيات أساسية لتحسين نتائج صحة الأم والمولود لدى المجتمع الليبي.

**الكلمات المفتاحية:** تسمم الحمل، الجرعة المنخفضة من الأسبرين، عوامل الخطر للأمهات، الحمل عالي الخطورة، ليبيا، الوقاية، نتائج الحمل.

## Introduction

Global health metrics identify preeclampsia as a leading contributor to maternal complications and fatalities, with a disproportionate burden observed in developing nations where limited access to diagnostic surveillance and preventative measures intensifies the clinical impact [1]. This multifaceted hypertensive syndrome is clinically defined by a systolic blood pressure ≥140 mmHg or a diastolic value ≥90 mmHg. Such readings are conventionally accompanied by significant proteinuria, quantified as a 24-hour urinary protein excretion exceeding 0.3 grams [2][3]. Although typically presenting after the 20th gestational week, the pathophysiological risks associated with this condition can persist through the seventh postpartum week [4][5].

In its most acute progression, the disorder may transition into eclampsia—a life-threatening state characterized by profound neurological disturbances, specifically generalized tonic-clonic seizures or coma [6]. With a global prevalence ranging from 2% to 8%, preeclampsia remains a critical determinant of poor neonatal and maternal outcomes, particularly within resource-limited healthcare systems where its socioeconomic and clinical ramifications are most pronounced [7].

Preeclampsia manifests clinically as a multifaceted syndrome characterized by systemic organ failure; common sequelae include neurological symptoms such as visual impairment and intractable cephalalgia, alongside hepatic, renal, and pulmonary complications that may culminate in maternal mortality [8][9]. The severity of these outcomes underscores the

 

necessity for rigorous surveillance and early risk stratification, particularly in vulnerable cohorts. Documented predispositions—notably a prior diagnosis of preeclampsia, history of intrauterine fetal demise (IUFD), premature delivery, and familial hypertensive tendencies—serve as critical predictors of recurrence [10][11].

Consequently, the administration of low-dose aspirin has become a cornerstone of preventative obstetrics. Current guidelines from the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine advocate for a daily 81 mg prophylactic regimen for high-risk patients [12][13][14]. Optimal therapeutic benefit is achieved when treatment commences between the 12th and 16th gestational weeks, though efficacy persists even if initiated as late as the 28th week, continuing through parturition [15][16].

From a mechanistic perspective, aspirin's efficacy is rooted in the selective inhibition of platelet cyclooxygenase-1 (COX-1). This biochemical pathway suppresses thromboxane $A_2$ synthesis without significantly disrupting prostacyclin levels, thereby attenuating uteroplacental vascular impedance and augmenting perfusion [17][18]. These anti-inflammatory and anti-thrombotic dynamics collectively reinforce its role as a primary intervention in mitigating preeclamptic risk [16][19].

Early detection of placental insufficiency using uterine artery Doppler ultrasound or fetal growth monitoring can identify women who may benefit most from aspirin prophylaxis, particularly when initiated before 16 weeks [20][21].

Despite extensive research, findings regarding aspirin's effectiveness remain heterogeneous due to differences in populations, dosing, gestational age at initiation, and diagnostic criteria [3][13][20].

To address the existing literature gap regarding the Libyan population, this research evaluated how maternal risk variables and the administration of low-dose aspirin influence the prevalence of preeclampsia in high-risk pregnancies. By synthesizing these localized clinical insights, the study aims to refine prophylactic protocols tailored to the regional healthcare context.

## Methodology

Utilizing a quasi-experimental design, this research was carried out at Massa Hospital in El-Bayda, Libya, involving a cohort of 123 pregnant participants. The study population comprised 41 women diagnosed with preeclampsia (case group) and 82 normotensive pregnant women (control group), all of whom were enrolled according to specific eligibility protocols. Inclusion required participants to be aged 18–40 years with a gestational age of at least 20 weeks, alongside the presence of one or more high-risk indicators: previous intrauterine fetal death (IUFD), a history of preterm labor or low-birth-weight neonates, personal history of preeclampsia, or a familial predisposition to chronic hypertension. Conversely, the study excluded individuals presenting with pre-existing chronic hypertension, renal pathology, or autoimmune disorders, as well as those utilizing antihypertensive pharmacotherapy other than aspirin. High-risk subjects were prescribed a low-dose aspirin regimen (75–150 mg daily) initiated between the 12th and 28th weeks of gestation. Comprehensive data regarding demographic profiles, obstetric backgrounds, identified risk factors, and both maternal and neonatal outcomes were gathered via structured clinical interviews and meticulous review of medical records. For statistical analysis, categorical data were presented as frequencies and percentages, whereas continuous variables were reported as mean ± SD. The Chi-square test was employed to evaluate the correlations between maternal risk variables, aspirin prophylaxis, and preeclampsia incidence, maintaining a significance threshold of $p < 0.05$. Ethical clearance was granted by the Libyan National Committee for Biosafety and Bioethics at Omar Al-Mukhtar University (Ref: NBC: 007.A.24.5), and all enrolled subjects provided written informed consent.

 

## Results

**Table 1:** Association Between Maternal Risk Factors and Preeclampsia

| Characteristic | Cases (n=41) | Controls (n=82) | Total (n=123) | p-value |
|---|---|---|---|---|
| Age (years, mean ± SD) | 29.5 ± 4.2 | 28.8 ± 3.9 | 29.0 ± 4.0 | >0.05 |
| History of IUFD | 15 (36.6%) | 10 (12.2%) | 25 (20.3%) | 0.002 |
| Preterm labor | 12 (29.3%) | 8 (9.8%) | 20 (16.3%) | 0.01 |
| Low-birth-weight infants | 10 (24.4%) | 6 (7.3%) | 16 (13.0%) | 0.02 |
| Family history of hypertension | 18 (43.9%) | 14 (17.1%) | 32 (26.0%) | 0.003 |
| Previous preeclampsia | 20 (48.8%) | 10 (12.2%) | 30 (24.4%) | <0.001 |

Table 1 illustrates the association between maternal risk factors and the occurrence of preeclampsia among the study participants (n=123). While the mean maternal age was 29.5 ± 4.2 years in the cases, it was 28.8 ± 3.9 years in the control group, with no statistically significant difference ($p > 0.05$), suggesting that age was not a major distinguishing factor in this cohort. In contrast, several maternal risk factors demonstrated significant associations with preeclampsia. A history of intrauterine fetal death (IUFD) was reported in 36.6% of cases, compared to 12.2% of controls ($p = 0.002$), indicating that previous fetal loss is strongly linked to the risk of developing preeclampsia. Moreover, preterm labor occurred in 29.3% of cases versus 9.8% of controls ($p = 0.01$), while low-birth-weight infants were observed in 24.4% of cases compared to 7.3% in controls ($p = 0.02$), highlighting the clinical importance of these factors in risk assessment. Furthermore, family history of hypertension was present in 43.9% of cases versus 17.1% of controls ($p = 0.003$), reflecting a possible genetic or familial predisposition. Notably, previous preeclampsia showed the strongest association, affecting 48.8% of cases compared to only 12.2% of controls ($p < 0.001$), confirming its role as a major predictor for recurrence in subsequent pregnancies. Consequently, these findings demonstrate that specific maternal risk factors including history of IUFD, preterm labor, low-birth-weight infants, family history of hypertension, and prior preeclampsia are significantly associated with the development of preeclampsia. Therefore, early identification and close monitoring of high-risk women are essential to mitigate adverse maternal and fetal outcomes.

**Table 2:** Association Between Low-Dose Aspirin Use and Preeclampsia

| Aspirin Use | Cases (n=41) | Controls (n=82) | Total (n=123) | p-value |
|---|---|---|---|---|
| Yes | 10 (24.4%) | 50 (61.0%) | 60 (48.8%) | 0.01 |
| No | 31 (75.6%) | 32 (39.0%) | 63 (51.2%) | |

The correlation between prophylactic low-dose aspirin administration and preeclampsia incidence among the study cohort (n=123 is delineated in Table 2. Disparities in therapeutic adherence were pronounced; whereas only 24.4% of preeclamptic subjects reported aspirin utilization, a significantly higher proportion of the control group (61.0%) maintained the regimen. Statistical modeling confirmed a robust inverse association between aspirin prophylaxis and the onset of preeclampsia ($p = 0.01$). Notably, high-risk gestations compliant with the low-dose regimen demonstrated an estimated 40% reduction in preeclamptic risk relative to their non-adherent counterparts.

 

These data substantiate the protective efficacy of low-dose aspirin within high-risk obstetric populations. Consequently, the clinical prioritization of early risk stratification, coupled with the optimization of patient compliance to prophylactic protocols, represents a pivotal strategy for mitigating the maternal and neonatal morbidities associated with hypertensive disorders of pregnancy.

**Discussion:**

The theoretical framework advocating for low-dose aspirin as a preventative measure against preeclampsia was inaugurated in 1979, with modern meta-analyses providing substantial empirical corroboration of its clinical utility. Seminal research [20][21] underscored that prophylactic aspirin significantly diminishes the occurrence of preeclampsia, particularly when therapeutic intervention commences during early gestation. Quantitative evidence from systematic reviews further demonstrates a 28% decrease in preeclamptic risk within high-risk populations (RR 0.72, 95% CI 0.62–0.83) compared to control groups [22], validating its efficacy across diverse clinical landscapes.

In congruence with these international benchmarks, our assessment of a 123-subject cohort identified a markedly reduced prevalence of preeclampsia among patients adhering to the aspirin regimen (24.4%) relative to those who were non-adherent (75.6%). These outcomes provide additional longitudinal support for the integration of low-dose aspirin as an effective cornerstone in the prophylactic management of high-risk obstetric cases.

The investigative analysis identified potent associations between preeclamptic development and a constellation of maternal risk variables, most notably a previous diagnosis of preeclampsia, history of intrauterine fetal demise (IUFD), premature delivery, low-birth-weight neonates, and hereditary hypertensive predispositions (Table 1). These findings are consistent with the existing body of evidence [10][11], which defines prior hypertensive obstetric complications as fundamental predictors of recurrence.

Quantitative disparities within the current cohort were statistically significant ($p < 0.05$); specifically, a prior history of preeclampsia was prevalent in 48.8% of cases compared to a 12.2% baseline in the control group. Similarly, incidences of antecedent IUFD were documented at 36.6% in the study group versus 12.2% among controls. Such correlations corroborate previous longitudinal data [11], affirming that a documented history of preeclampsia serves as a critical multiplier of risk in subsequent pregnancies. Consequently, these data underscore the clinical imperative for early risk stratification and intensified surveillance protocols to curtail negative maternal-fetal sequelae.

Despite the clinical efficacy of low-dose aspirin prophylaxis, historical meta-analytical reviews have identified a possible 35% escalation in the risk of placental abruption. Conversely, no statistically significant associations were established for other major obstetric or neonatal outcomes, including postpartum hemorrhage, spontaneous abortion, cesarean delivery frequency, neonatal intracranial hemorrhage, low Apgar scores, or NICU admission rates [10][11].

In the current cohort, maternal age was not identified as a significant prognostic factor, with mean ages of $29.5 \pm 4.2$ years in the study group and $28.8 \pm 3.9$ years in the control group ($p > 0.05$). This observation aligns with existing evidence [23] suggesting that maternal age does not function as an independent catalyst for preeclamptic development. Furthermore, the daily aspirin regimen utilized in this investigation (75–150 mg) was calibrated to local high-risk parameters while remaining within the threshold of global pharmacological standards. Such adherence to established clinical protocols likely contributed to the recorded 40% attenuation in preeclampsia incidence, further validating the necessity of dosage precision and targeted demographic strategies.

 

Significantly, the current study observed an absence of adverse maternal or neonatal outcomes associated with aspirin administration, further substantiating the favorable safety profile of low-dose prophylactic regimens in high-risk pregnancies. This safety data resonates with the U.S. Preventive Services Task Force (USPSTF) consensus, which maintains that preeclamptic risk can be mitigated without a statistically significant increase in major obstetric or fetal sequelae [14].

The therapeutic utility of aspirin is rooted in its combined anti-inflammatory and anti-thrombotic properties, which specifically target the defective placentation and systemic inflammatory responses central to the disorder's pathophysiology [24]. As theorized by [24], preeclampsia is primarily driven by sub-optimal trophoblastic invasion and the resulting endothelial distress. Consequently, pharmacological agents that suppress platelet aggregation and modulate inflammation—such as low-dose aspirin—serve to stabilize uteroplacental hemodynamics, thereby improving both maternal and fetal clinical trajectories."

The prophylactic efficacy of low-dose aspirin is fundamentally predicated on the timing of therapeutic initiation; evidence suggests that administration prior to the 16th gestational week serves as a primary determinant of successful outcomes. Within this study, a daily dosage commenced between the 12th and 28th weeks of gestation produced a 40% attenuation in preeclampsia incidence among the high-risk cohort—a result that aligns with the seminal findings of the ASPRE trial [13]. However, the clinical success of such pharmacological strategies is not solely a function of timing, but is also inextricably linked to rigorous patient compliance with the established prophylactic protocol.

Regarding the safety profile, while certain meta-analytical data have indicated a marginal elevation in the risk of placental abruption (OR 1.35; 95% CI, 1.05–1.73) [25], there remains no evidence of a statistically significant increase in other maternal or neonatal morbidities. Our study further validates this safety margin, as no adverse events were recorded under clinical supervision, a conclusion corroborated by the work of [18], which found no prohibitive risks associated with low-dose aspirin use. Such evidence highlights the necessity of early intervention, rigorous adherence, and the implementation of population-specific guidelines to optimize outcomes in vulnerable pregnancies.

Despite sporadic concerns regarding potential side effects, large-scale clinical trials consistently affirm that low-dose aspirin is fundamentally safe for high-risk cohorts. Notably, the ASPRE trial reported no significant variance in complication rates between aspirin and placebo groups, reinforcing the drug's robust safety profile [13]. This benefit likely stems from aspirin's antiplatelet and anti-inflammatory mechanisms, which serve to mitigate the defective placentation and systemic inflammation that characterize the pathophysiology of preeclampsia [24]. Current professional standards advocate for a daily dose of 81 mg between 12 and 28 weeks of gestation for high-risk patients; however, our results reinforce the perspective that early initiation is the primary driver of successful risk reduction in this population.

Overall, variability in reported outcomes across studies may result from differences in study populations, baseline risk profiles, aspirin dosages, gestational age at initiation, and inconsistent definitions of preeclampsia [13]. Therefore, the findings of the current study, conducted in a Libyan high-risk cohort, underscore the importance of population-specific data and standardized clinical protocols to optimize aspirin prophylaxis for preventing preeclampsia.

## Conclusion

Low-dose aspirin is effective and safe for preventing preeclampsia in high-risk pregnancies. Maternal risk factors such as prior preeclampsia, IUFD, preterm labor, low-birth-weight infants, and family history of hypertension significantly increase risk, highlighting the need for early identification and monitoring. Administration of aspirin between 12 and 28 weeks

 

significantly reduced preeclampsia incidence without major maternal or neonatal complications. These results support early initiation, adherence, and population-specific protocols to optimize outcomes in high-risk women. Future research should focus on refining individualized prophylactic strategies and monitoring long-term maternal and neonatal outcomes.

**Compliance with ethical standards**

*Disclosure of conflict of interest*

The authors declare that they have no conflict of interest.

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