

# Gaps in Low-Dose Aspirin Use for Preeclampsia Prevention: Insights and Clinical Implications

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**Objective:** To evaluate real-world prescribing patterns of low-dose aspirin for preeclampsia prevention among pregnant women who met the Israeli or American College of Obstetricians and Gynecologists (ACOG) guideline criteria for preeclampsia prophylaxis, and to identify disparities and missed opportunities in implementing risk-based prophylaxis in a diverse obstetric population.

**Methods:** This retrospective study analyzed women who delivered live births at a tertiary medical center in northern Israel between March 2020 and April 2024. Eligibility for low-dose aspirin prophylaxis was assessed using Israeli guidelines, focusing on major risk factors, and the broader ACOG criteria, which include moderate-risk factors. This dual approach reflects debates in Israel about incorporating moderate-risk factors into routine clinical practice.

**Results:** Of 18,838 women included, 1,160 (6.2%) met the criteria for low-dose aspirin prophylaxis under Israeli guidelines, and 511 (44.1%) of these received prescriptions. The prescription rate was highest among women with a history of preeclampsia (79.0%) and pregestational diabetes (66.3%) but notably lower among those with chronic hypertension (30.3%) and autoimmune diseases (41.3%). Under ACOG criteria, 2,559 women (13.6%) were eligible for low-dose aspirin, but only 27.9% (715/2,559) received prophylaxis. The prescription rate was significantly higher among women with high-risk factors than among those with only moderate-risk factors (OR=0.16,  $p<0.001$ ). Arab women were more likely to receive low-dose aspirin than were Jewish women (31.2% vs 24.5%,  $p<0.001$ ), consistent with higher prevalences of risk factors. Multivariate analysis showed that a history of preeclampsia (OR=7.15,  $p<0.001$ ) and pregestational diabetes (OR=3.80,  $p<0.001$ ) were strongly associated with low-dose aspirin prescription.

**Conclusion:** Our findings reveal suboptimal prescription of low-dose aspirin according to guideline criteria, especially among women with moderate-risk factors. Even among women with high-risk factors, disparities in prescribing practices persisted. These gaps highlight the need for better provider education, consistent risk assessment, and structured implementation strategies to improve guideline adherence.

**Keywords:** low-dose aspirin, preeclampsia, preeclampsia prevention

## Introduction

Preeclampsia is a hypertensive disorder of pregnancy that typically develops after 20 weeks of gestation and contributes substantially to maternal and perinatal morbidity and mortality. Its pathophysiology involves abnormal placentation, endothelial dysfunction, and immune system dysregulation.<sup>1-4</sup> Low-dose aspirin (LDA) prophylaxis has been shown to reduce the incidence of preterm preeclampsia by up to 62% in high-risk populations when initiated between 12 and 16 weeks of gestation at a dose of 150 mg.<sup>5</sup> The proposed mechanisms of this treatment include inhibition of thromboxane synthesis, improved placental blood flow, decreased platelet aggregation, and modulation of inflammatory pathways.<sup>6,7</sup> The American College of Obstetricians and Gynecologists (ACOG) and other leading organizations recommend LDA for pregnant women at high risk for preeclampsia.<sup>5,6</sup>

The Israeli Society of Maternal Fetal Medicine adopted elements of the ACOG guidelines,<sup>8</sup> recommending LDA prophylaxis for women with major risk factors such as chronic hypertension and pregestational diabetes, and twin pregnancies, thus aligning these guidelines with local clinical practice.<sup>9-11</sup> Nonetheless, there is ongoing debate in Israel

regarding the extent to which the broader ACOG criteria, including moderate-risk factors, should be implemented in routine clinical practice.<sup>9</sup> The Israeli guidelines primarily emphasize major risk factors. However, it remains unclear whether some clinicians also consider moderate-risk factors, which would lead to potential variations in the application of LDA prophylaxis.<sup>12</sup> This debate reflects differing interpretations of the evidence and highlights the need for a deeper understanding of current practices across healthcare providers.

Our medical center, a tertiary university-affiliated hospital in Israel's periphery, serves a diverse population of over 600,000 individuals, including both Jewish and Arab communities. In this retrospective study, we sought to assess adherence to LDA prophylaxis guidelines, comparing prescribing practices based on two distinct sets of criteria: the local Israeli guidelines and the broader ACOG recommendations. This study specifically addressed the extent to which pregnant women who met either the Israeli or ACOG criteria for LDA were actually prescribed treatment, and identified the characteristics of those who were not treated within a diverse Israeli population. By identifying characteristics of pregnant women who were not prescribed LDA despite meeting either set of criteria, this study aimed to highlight gaps in guideline implementation and support efforts to optimize preventive care practices for preeclampsia. Although previous studies have documented suboptimal adherence to aspirin prophylaxis, our goal was to examine these patterns in a diverse Israeli population and to explore barriers to implementation. Moreover, the specific impact of guideline differences is less well understood and may help explain real-world variability in clinical practice.

## Methodology

In a retrospective study conducted at Galilee Medical Center, we included all the live births occurring between March 2020 and April 2024. The primary outcome of this study was the rate of LDA prescription among pregnant women who met the eligibility criteria for treatment according to Israeli and ACOG guidelines. Eligibility for LDA prophylaxis was assessed using two approaches: local Israeli guidelines<sup>9–11</sup> and the ACOG Committee Opinion No. 743: “Low-Dose Aspirin Use in Pregnancy”.<sup>8</sup>

The Israeli guidelines emphasize high-risk factors, including a history of preeclampsia, especially when accompanied by an adverse outcome. Other high-risk factors include: chronic hypertension, type 1 or type 2 diabetes, renal disease, autoimmune diseases such as systemic lupus erythematosus and antiphospholipid syndrome,<sup>9</sup> advanced maternal age ( $\geq 45$  years),<sup>10</sup> and multifetal gestation with additional risk factors. The latter include high BMI ( $\geq 35$  kg/m<sup>2</sup>), maternal age  $\geq 40$  years, nulliparity, in vitro fertilization (IVF), and personal history factors such as low birth weight, small for gestational age, previous adverse pregnancy outcome, and  $>10$ -year pregnancy interval.<sup>11</sup>

The ACOG criteria recommend LDA prophylaxis for women with one high-risk factor or at least two moderate-risk factors.<sup>8</sup> High-risk factors include: a history of preeclampsia, multifetal gestation, chronic hypertension, type 1 or 2 diabetes, renal disease, and an autoimmune disease, such as systemic lupus erythematosus or antiphospholipid syndrome. The moderate risk factors included: nulliparity, obesity (body mass index  $>30$  kg/m<sup>2</sup>), age 35 years or older, and personal history factors. The latter include: low birth weight, small for gestational age, a previous adverse pregnancy outcome,  $>10$ -year pregnancy interval, and IVF. Given the retrospective study design, certain risk factors were inconsistently or inadequately recorded in the prenatal records. Consequently, variables such as a family history of preeclampsia in a first-degree relative, low socioeconomic status, and black race were not considered.

Women who met the eligibility criteria and had a prescription for LDA prophylaxis were classified as having been prescribed “appropriate prophylaxis”. Women who met the criteria for prophylactic treatment but did not have evidence of an LDA prescription were categorized as having “missed prophylaxis”. Prescription status was based on documentation in the prenatal and hospital records; data on whether the medication was actually dispensed or taken were not available.

In addition to assessing the prescription of LDA prophylaxis, we collected data on the incidence of preeclampsia and severe preeclampsia, as documented in the medical records at the time of delivery. These outcomes were recorded to provide information on the frequency of hypertensive complications within the study cohort. We did not collect data on additional maternal or neonatal outcomes, as this was beyond the scope of our study, which was primarily focused on evaluating prescription patterns in relation to guideline-based prophylaxis. Major fetal anomalies were identified using ICD-10 codes and confirmed by manual chart review; and women were excluded from the analysis if the anomaly was

likely to impact pregnancy management or outcomes. Missing data were defined as the absence of essential clinical variables needed to determine eligibility for LDA or document prescription status.

Documentation of low-dose aspirin prophylaxis was based on provider records and reflects prescriptions or recommendations, not confirmed patient intake. Pharmacy or patient-reported data were unavailable.

Qualitative variables are displayed as frequencies and percentages. Categorical variables were assessed using Pearson's chi-squared test or Fisher's exact test, with statistical significance defined by a two-tailed p-value of <0.05. To evaluate the relation between specific preeclampsia risk factors and the likelihood that LDA was prescribed, a multinomial logistic regression was applied. The rationale for this analysis was to assess the degree to which the presence of specific clinical risk factors, which were included in the definition of eligibility for LDA, were associated with actual prescription. This enabled evaluating real-world adherence to guideline-based recommendations and identifying factors most strongly linked with implementation. The results are presented as odds ratios (OR) or adjusted odds ratios (aOR) with 95% confidence intervals (CI). All the statistical analyses were performed using SPSS software, version 27.0 (IBM Corp., Armonk, NY, USA).

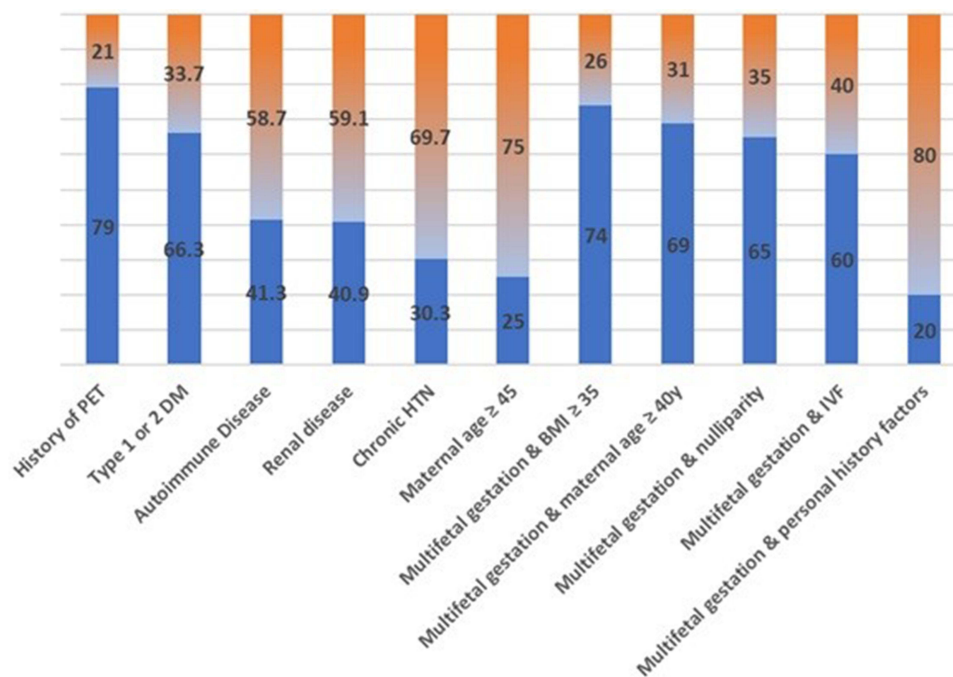
## Results

During the study period, 19,620 women delivered at Galilee Medical Center. After 782 were excluded due to severe fetal anomalies or incomplete data, a total of 18,838 women were included in the analysis.

### The Utilization of LDA Prophylaxis According to Israeli Guidelines

A total of 1,160 women were classified as eligible for aspirin prophylaxis according to the Israeli guidelines. Of these, 511 (44.1%) received aspirin as recommended. Conversely, among the 17,678 women who were not eligible, 829 (4.7%) received aspirin despite not meeting the criteria.

Among the women with the highest prescription rates for aspirin prophylaxis, 79.0% (94/119) of those with a history of preeclampsia were prescribed aspirin, followed by 66.3% (67/101) of those with pre-gestational diabetes. In contrast, the lowest prescription rates were observed among women with autoimmune diseases (41.3%, 64/155) and chronic hypertension (30.3%, 148/489). [Figure 1](#) illustrates the rates of LDA prophylaxis across various risk factors according to Israeli guidelines.



**Figure 1** Prescription rates of low-dose aspirin among 1,160 pregnant women eligible under Israeli guidelines. Blue bars represent the percentages of women with each risk factor who were prescribed low-dose aspirin; Orange bars represent those not prescribed. The percentages shown on each bar reflect the proportions that received versus did not receive a prescription.

**Abbreviations:** PET, preeclampsia; DM, diabetes mellitus; HTN, hypertension; IVF, in vitro fertilization.

The prescription rate of LDA varied by the number of risk factors. The rate was 40.7% (395/971) among women with one risk factor, and increased to 61.9% (99/160) for two risk factors and 55.6% (15/27) for three risk factors. The prescription rates did not differ significantly between eligible Arab and Jewish women: 45.2% (325/719) vs 42.6% (179/420),  $p=0.422$ .

In a multivariate regression analysis, a history of preeclampsia was significantly associated with a LDA prescription, with an OR of 7.15 (95% CI: 4.201–12.150,  $p<0.001$ ). Similarly, pre-gestational diabetes was significantly associated, with an OR of 3.80 (95% CI: 2.263–6.393,  $p<0.001$ ). Conversely, chronic hypertension, renal disease, autoimmune disease, and multifetal gestation combined with IVF were not significantly associated with LDA prophylaxis prescriptions (Table 1).

## LDA Prophylaxis Prescription According to ACOG Guidelines

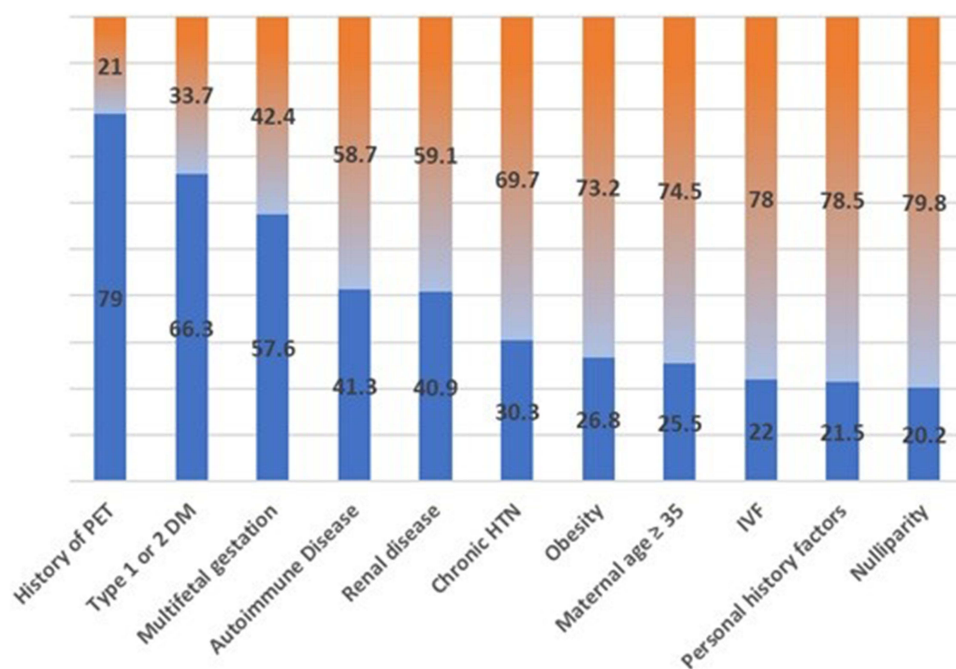
Of the total cohort, 2,559 women (13.6%) were eligible for LDA prophylaxis based on ACOG criteria. Among them, 715 (27.9%) received appropriate prescriptions. Of the 16,279 women who did not meet ACOG criteria, 625 (3.8%) were prescribed LDA. Prescription rates were highest among women with a history of preeclampsia (79.0%, 94/119) and type 1 or 2 diabetes mellitus (66.3%, 67/101). Lower rates were observed among those with chronic hypertension (30.3%, 148/489), obesity (26.8%, 114/425), and advanced maternal age (25.5%, 306/1,199) (Figure 2). Table 2 demonstrates LDA prophylaxis rates across various combinations of high- and moderate-risk factors. The prescription rate was 54% (95/177) among women with one high- and two moderate-risk factors, and increased to 61% (23/38) among those with one high- and three moderate-risk factors. Among women with two high-risk factors and no moderate-risk factors, the prescription rate was 57% (30/53). Women with no high-risk factors but multiple moderate-risk factors were significantly less likely to be prescribed LDA than were women with at least one high-risk factor (OR: 0.16, 95% CI: 0.131–0.198,  $p<0.001$ ).

Higher proportions of Arab than Jewish women had at least one high-risk factor for preeclampsia (57% vs 43%,  $p<0.001$ ), and two or more high-risk factors (7.4% vs 4.2%,  $p<0.001$ ). This difference likely explains the higher prescription rate of LDA prophylaxis among Arab than Jewish women: 31.2% (441/1,412) vs 24.5% 266/1,086,  $p<0.001$ ).

**Table 1** Independent Relations Between Specific Risk Factors and Low-Dose Aspirin Prophylaxis Among 1,160 Women Eligible for Treatment According to Israeli Guidelines. Adjusted Odds Ratios with 95% Confidence Intervals and p Values are Shown

High-Risk Factors	Adjusted OR	95% CI Lower	95% CI Upper	P Value
History of PET	7.145	4.201	12.15	<0.001
Pre-gestational DM	3.803	2.263	6.393	<0.001
Chronic hypertension	0.684	0.457	1.024	0.065
Renal disease	1.117	0.747	1.669	0.589
Autoimmune disease	1.184	0.78	1.796	0.427
Maternal age $\geq$ 45 years	0.628	0.063	6.247	0.692
Multifetal gestation and maternal age $\geq$ 40 years	2.574	0.831	7.972	0.101
Multifetal gestation and BMI $\geq$ 35	2.669	1.06	6.721	0.037
Multifetal gestation and personal history factors	6.998	1.42	34.497	0.017
Multifetal gestation and nulliparity	2.751	1.682	4.5	<0.001
Multifetal gestation and IVF	1.512	0.889	2.574	0.127

**Abbreviations:** OR, odds ratio; CI, confidence interval; PET, preeclampsia; DM, diabetes mellitus; BMI, body mass index; IVF, in vitro fertilization.



**Figure 2** Prescription rates of low-dose aspirin among 2,559 pregnant women eligible under the American College of Obstetricians and Gynecologists guidelines, stratified by combinations of high- and moderate-risk factors. Blue bars represent the percentages of women with each risk factor combination who received a prescription; Orange bars represent those who did not. The percentages shown on each bar reflect the proportions within each subgroup.

**Abbreviations:** PET, preeclampsia; DM, diabetes mellitus; HTN, hypertension; BMI, body mass index; IVF, in vitro fertilization.

**Table 3** illustrates the independent relations between specific risk factors and LDA prophylaxis prescriptions. High-risk factors, including autoimmune disease, renal disease, multifetal gestation, a history of preeclampsia, chronic hypertension, and type 1 or 2 diabetes were all significantly associated with increased LDA prophylaxis prescriptions during pregnancy ( $p < 0.05$  for all). However, some moderate risk factors, namely nulliparity, personal history factors, and IVF were not significantly associated with LDA prophylaxis prescriptions.

Preeclampsia occurred in 144 out of 715 women (20.1%) who were prescribed LDA prophylaxis compared to 110 out of 1844 women (6.0%) who were not prescribed. The OR was 3.975 (95% CI: 3.048–5.185,  $p < 0.01$ ). Severe preeclampsia was observed in 23 of 715 women (3.2%) in the LDA group, compared to 22 of 1844 women (1.2%) in the

**Table 2** Prescription Rates of Low-Dose Aspirin Prophylaxis Among 2,559 Women Eligible for Treatment According to American College of Obstetricians and Gynecologists Criteria, Stratified by the Number of High- and Moderate-Risk Factors. The Data are Presented as the Number That Received a Prescription Relative to the Total Number in Each Subgroup, with the Corresponding Percentage in Parentheses

Number of high-risk factors	Number of Moderate Risk factors				
	0	1	2	3	4
0	NA	NA	114/1101 (10)	25/153 (16)	4/11 (36)
1	157/392 (40)	202/533 (38)	95/177 (54)	23/38 (61)	3/3 (100)
2	30/53 (57)	29/49 (59)	15/27 (56)	8/9 (89)	1/2 (50)
3	1/1 (100)	6/9 (67)	8/9 (89)	0	0
4	0	1/1 (100)	0	0	0

**Table 3** Independent Associations Between Specific High- and Moderate-Risk Factors and Prescription Rates of Low-Dose Aspirin Among 2,559 Women Eligible for Treatment According to American College of Obstetricians and Gynecologists Criteria. The Data Include the Number of Women Who Received or Did Not Receive Low-Dose Aspirin, Adjusted Odds Ratios (aOR), 95% Confidence Intervals, and p Values for Each Factor

		No LDA Prophylaxis (n=209)	LDA Prophylaxis (n=92)	aOR	95% CI Lower	95% CI Upper	P Value
<b>High-risk factors</b>	<b>Autoimmune disease</b>	91 (4.9%)	64 (9.0%)	3.003	2.005	4.497	<0.001
	<b>Renal disease</b>	149 (8.1%)	103 (14.4%)	3.549	2.522	4.995	<0.001
	<b>Multifetal gestation</b>	146 (7.9%)	198 (27.7%)	10.983	8.118	14.858	<0.001
	<b>History of PET</b>	25 (1.4%)	94 (13.1%)	25.795	15.546	42.803	<0.001
	<b>Chronic hypertension</b>	341 (18.5%)	148 (20.7%)	2.705	2.036	3.593	<0.001
	<b>Type 1 or 2 DM</b>	34 (1.8%)	67 (9.4%)	13.348	8.329	21.391	<0.001
<b>Moderate risk factors</b>	<b>Obesity</b>	311 (16.9%)	114 (15.9%)	1.544	1.166	2.046	0.002
	<b>Nulliparity</b>	993 (53.9%)	252 (35.2%)	0.909	0.726	1.138	0.403
	<b>Personal history factors</b>	227 (12.3%)	64 (9.0%)	1.096	0.766	1.568	0.617
	<b>Age 35 years or older</b>	893 (48.4%)	306 (42.8%)	1.562	1.25	1.951	<0.001
	<b>IVF</b>	554 (30.0%)	152 (21.3%)	1.254	0.973	1.617	0.08

**Abbreviations:** LDA, low dose aspirin; Aor, adjusted odds ratio; CI, confidence interval; PET, preeclampsia; DM, diabetes mellitus; IVF, in vitro fertilization.

non-aspirin group. The OR was 2.753 (95% CI: 1.524–4.971,  $p=0.001$ ). No association was found of LDA prophylaxis with preeclampsia or with severe preeclampsia before 32 weeks of gestation.

## Discussion

We report a low prescribing rate of LDA prophylaxis among women who met the criteria delineated in existing guidelines. High-risk factors were significantly associated with an increased likelihood of receiving LDA during pregnancy. However, women with multiple moderate risk factors but not a high-risk factor were 84% less likely than those with a high-risk factor to be prescribed LDA (OR=0.16, 95% CI 0.13–0.2,  $p<0.001$ ).

Aspirin, or acetylsalicylic acid, is well established for its anti-inflammatory and antithrombotic properties. At low doses, it irreversibly inhibits the COX-1 enzyme, reducing thromboxane A2 production, which is a potent vasoconstrictor, and promotes platelet aggregation.<sup>10</sup> This mechanism is believed to improve placental blood flow and decrease the risk of hypertensive disorders in pregnancy, particularly preeclampsia.<sup>11</sup> Despite the incomplete understanding of the precise pathways by which LDA prevents preeclampsia, it remains a key intervention for women at high risk. In 2018, the ACOG, in collaboration with the Society for Maternal-Fetal Medicine, recommended daily LDA for women at high risk of preeclampsia, starting between 12 and 28 weeks of gestation, ideally before 16 weeks, and continuing until delivery. Additionally, LDA is recommended for women with multiple moderate-risk factors, such as advanced maternal age or nulliparity.<sup>8</sup> The Israeli Society of Maternal Fetal Medicine partially adopted these guidelines, emphasizing LDA prophylaxis for women with major risk factors, such as chronic hypertension and pregestational diabetes, while incorporating some elements related to moderate-risk factors.<sup>9–11</sup> As LDA should ideally be started at 12 to 16 weeks of gestation, it is often prescribed by general obstetricians in the community, who are typically the first to treat pregnant women. This highlights the need for targeted educational initiatives for these providers to enhance adherence to prophylaxis guidelines.

Our findings align with reports from other countries, of low prescribing and use of LDA prophylaxis despite guidelines.<sup>12–15</sup> For example, a US study by Krishnamurti et al revealed that 27.4% of women at high risk for preeclampsia had no mention of LDA in their medical records, and among those with documented recommendations, 36.7% were unaware of the need for LDA.<sup>14</sup> These findings highlight significant gaps in both risk identification and

communication between healthcare providers and patients. Our finding that women with moderate-risk factors compared to those with high-risk were less likely to be prescribed LDA, corroborates other reports, and raises an opportunity for intervention in this subgroup.<sup>16,17</sup> Moreover, our study showed that Arab women were more commonly prescribed LDA, reflecting their higher prevalence of risk factors for preeclampsia. This suggests that specific subpopulations, such as Arab women, may benefit from focused efforts to prevent preeclampsia. Although there is ongoing debate in Israel regarding the criteria that should guide aspirin prophylaxis, our findings suggest that suboptimal prescribing persists regardless of whether the narrower Israeli or the broader ACOG criteria are applied. This indicates that prescription rates may be less dictated by the choice of criteria, and more by gaps in implementation. Understanding that both approaches yielded similarly low prescribing rates supports the need for system-level interventions—such as provider education, clearer risk assessment protocols, and early identification strategies—regardless of the guideline that is ultimately followed.

An intriguing finding in our study was the higher incidence of preeclampsia among women who received LDA. This may be due to selection bias, by which women at higher risk were more likely to be prescribed LDA. Other factors, such as inappropriate dosing or non-adherence, could have also contributed. Reverse causality should also be considered. Specifically, subtle early signs of evolving disease, such as mildly rising blood pressure, may have prompted clinicians to initiate aspirin treatment even within the recommended gestational window. Additionally, unmeasured confounders may have influenced both the decision to prescribe LDA and the actual risk of developing preeclampsia. Adherence to LDA was not assessed in our study, which may have limited its protective effect. Although current guidelines recommend initiating LDA ideally between 12 and 16 weeks of gestation, it remains acceptable to begin treatment as late as 28 weeks. However, in our cohort, precise data regarding the actual timing of initiation were unavailable, and such variability may have influenced the observed outcomes. Moreover, information on the type of provider (eg, community obstetrician versus maternal-fetal medicine specialist) and care delivery model was not available, though these factors may also influence prescribing behavior and contribute to practice variation.

Notably, the method currently used in Israel to identify candidates for aspirin prophylaxis—based solely on clinical risk factors—may not be optimal. Prescription that is based solely on clinical risk factors—such as maternal age, parity, BMI, and medical or obstetric history—is limited in its ability to identify women at risk for preeclampsia, and the detection of preterm preeclampsia is about 60%.<sup>11</sup> In contrast, incorporating biochemical and biophysical markers, including mean arterial pressure, uterine artery Doppler, PAPP-A, and PIGF, significantly improves prediction. This combined approach, as applied in the ASPRE trial, enables earlier and more accurate identification of high-risk women, this yielding targeted aspirin use and achieving a substantially greater reduction in preeclampsia incidence.<sup>5</sup> However, in Israel, this screening algorithm is not currently implemented in routine clinical practice, and risk assessment remains primarily based on clinical criteria. It is important to note that our study was not designed to evaluate the effectiveness of LDA in preventing preeclampsia; therefore, these findings should be interpreted with caution and warrant further investigation.

The strengths of our study include the large sample size and the real-world clinical setting, which support the robustness and clinical relevance of our findings. The large cohort enabled examining current LDA prescribing practices across diverse patient populations. Furthermore, our assessment of prescription rate according to both Israeli and ACOG guidelines provided a unique opportunity to evaluate differences in prescribing practices based on national and international recommendations. Stratifying LDA use by risk categories helped identify potential gaps in prophylaxis, particularly in moderate-risk groups, in which adherence to guidelines may be more variable. Although the regression model included risk factors already defined by the guidelines, it was applied to assess whether these factors were indeed associated with real-world prescription, thus highlighting potential gaps in implementation. Potential misclassification bias, unmeasured confounders, and lack of dose validation are limitations that must be considered due to the retrospective study design. Moreover, incomplete or missing information, especially regarding certain risk factors that were not consistently recorded in medical charts should also be considered. This limitation may have introduced selection or information bias, particularly in identifying all the women eligible for LDA prophylaxis. These include incomplete or missing information, especially regarding certain risk factors that were not consistently recorded in medical charts. The single-center design also limits the generalizability of our findings, as the prescribing practices and patient demographics at our institution may not reflect those in other regions or healthcare settings. Additionally, we were unable to assess

adherence to aspirin therapy, as direct confirmation of intake (eg, pharmacy dispensing data or patient self-report) was not available. Our data therefore reflect prescribing behavior rather than confirmed use, which may result in either over- or under-estimation of actual adherence. This limitation should be considered when interpreting the identified gaps in clinical practice. Moreover, data on the exact dose were unavailable, although doses in Israel range between 75 and 150 mg. As explained above, we did not collect data on obstetric or neonatal outcomes, other than on incidences of preeclampsia. Regardless, our ability to draw conclusions about the clinical effectiveness of aspirin prophylaxis is limited by the low prescription rate of aspirin and the likely bias in provider decision-making regarding whom to treat.

This study may be viewed as a real-world audit of aspirin prescribing practices in a tertiary Israeli center. While suboptimal adherence to LDA guidelines has been documented elsewhere, our findings contextualize this issue within a local healthcare system that incorporates both national and international recommendations. By identifying population-specific patterns and potential barriers to implementation, such as ambiguity in criteria and lack of provider awareness, this work contributes insight to the global conversation on preeclampsia prevention. To enhance adherence to LDA guidelines, we recommend integrating standardized risk assessment tools into early prenatal visits, supported by decision aids or electronic alerts within clinical software. Educational initiatives targeting community-based providers—who are most often responsible for initiating LDA—could improve early identification and prescription. Additionally, national efforts to harmonize guideline implementation and to consider inclusion of biochemical or Doppler markers, as in the ASPRE model,<sup>11</sup> may further refine risk stratification and improve prophylaxis.

In conclusion, the rate of LDA prophylaxis for preeclampsia prevention in our population was low. Our findings underscore the need for a more structured approach to identifying and managing women at risk for preeclampsia. The low adherence to LDA guidelines indicates gaps in clinical practice, which could be addressed through provider education, systematic risk assessment tools, and clearer treatment protocols. Future efforts should focus on refining risk assessment, improving physician awareness of LDA recommendations, and ensuring early initiation of prophylaxis within the critical gestational window.

## Abbreviations

LDA, low-dose aspirin; ACOG, The American College of Obstetricians and Gynecologists; IVF, in vitro fertilization.

## Data Sharing Statement

Data may be obtained from the corresponding author (I.S) upon reasonable request.

## Ethics Approval and Consent to Participate

Our study was performed in compliance with the Declaration of Helsinki. The protocol of the study was approved by the local Institutional Review Board (Helsinki Committee) of the Galilee Medical Center, Nahariya, Israel (number of approval NHR-23-186). The need for written informed consent was waived because of the retrospective study design. All the data were anonymized to ensure patient confidentiality.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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