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Efficacy and Safety of Aspirin 162 mg for Preeclampsia Prophylaxis in High-Risk Patients

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Abstract

Objective The aim of this study was to compare the safety and efficacy of aspirin 162 mg to the standard recommended dose of 81 mg for preeclampsia prevention.

Study Design A retrospective cohort study of patients at risk for preeclampsia who delivered between January 2013 and December 2020 at Henry Ford Health was performed. Patients were divided into three groups: a no aspirin group, a group treated under an 81 mg aspirin preeclampsia prophylaxis protocol, and a group treated under a 162 mg protocol. Univariate and multivariable logistic regression analyses compared rates of preeclampsia and secondary outcomes between groups. Clinical side effects traditionally associated with aspirin use were also assessed.

Results Of 3,597 patients, 2,266 (63%) were in the no aspirin group, 944 (26%) were in the 81 mg group, and 387 (11%) were in the 162 mg group. The rate of preeclampsia was significantly lower in the 162 mg group (10.1%, odds ratio, 0.68; 95% confidence interval, 0.46–0.99) compared with the 81 mg group (14.2%). The rate of preeclampsia was identical in the no aspirin and 81 mg groups. The rate for postpartum hemorrhage, postpartum hematoma, and intraventricular hemorrhage of the newborn were not significantly different between patients in the 162 and 81 mg groups.

Conclusion We observed a significantly lower rate of preeclampsia in high-risk patients who were treated with the 162 mg dose of aspirin for preeclampsia prophylaxis, and bleeding complications were not seen with the higher dose. Our study suggests that aspirin 162 mg may be considered for prophylaxis in patients at high risk for preeclampsia.

Keywords
- preeclampsia
- aspirin
- prophylaxis
- high-risk pregnancies

Key Points

- Aspirin 81 mg is currently standard for preeclampsia prophylaxis.
- Preeclampsia rate is significantly lower among high-risk patients taking aspirin 162 mg compared with 81 mg.
- Bleeding complications are not increased among those taking aspirin 162 mg.

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Preeclampsia is a disorder of pregnancy associated with new-onset hypertension occurring after 20 weeks of gestation.[1] Preeclampsia affects 2 to 8% of all pregnancies and can cause significant maternal morbidity and mortality.[2,3] It is also associated with significant neonatal morbidity, including premature birth and fetal growth restriction.[4] Several etiologic mechanisms for preeclampsia have been suggested, including uteroplacental ischemia, trophoblast apoptosis, immune maladaptation, and genetic imprinting.[5–7] More recent studies have examined the role of angiogenic factor imbalances in preeclampsia,[8,9] and others have proposed that an imbalance in prostacyclin and thromboxane A2 metabolism may be involved in the pathogenesis of preeclampsia.[10,11] These studies led to investigations of aspirin for the prevention of preeclampsia, since it is a prostaglandin synthesis inhibitor that reduces levels of thromboxane A2 at low doses.[10,11]

Several studies have evaluated the prophylactic use of aspirin for decreasing the risk of preeclampsia, and these studies have varied widely in regard to population risk profiles, aspirin dosage, gestational age of prophylaxis initiation, and preeclampsia risk definition.[12] Additionally, many of these studies were performed in different countries, so the true aspirin doses may have varied because of differing manufacturing practices and drug formulations in those regions. Many seminal aspirin studies were conducted in Europe and the United Kingdom, where aspirin is available in 75 and 300 mg tablets, and these studies have shown safety and efficacy for preeclampsia prevention at the dose of 150 mg. However, aspirin in the United States is produced in 81 and 325 mg tablets, making the 150 mg recommended dose difficult to accurately comply with. Nonetheless, in 2014, the U.S. Preventive Services Task Force (USPSTF) published guidelines for the use of low-dose aspirin to prevent morbidity and mortality from preeclampsia,[13] and the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) supported these guidelines.[14] Currently, the ACOG recommendation for preeclampsia prevention is low-dose aspirin of 81 mg per day in patients who are at risk, which is substantially lower than the 150 mg dose which was shown to be safe and effective.[1] While many studies have explored the use of low-dose aspirin for preventing preeclampsia, few studies have explored the impact of a higher 162 mg dose for this indication.

The aim of this study was to assess whether prophylactic use of aspirin at 162 mg in patients with preeclampsia high-risk factors would be associated with a lower rate of preeclampsia and other perinatal complications than with use of aspirin at the current standard dose of 81 mg.

Materials and Methods

We performed a retrospective pre-post cohort study of pregnant women who were at risk of preeclampsia and who delivered at Henry Ford Health (HFH) between January 2013 and December 2020 during three time periods that included two different prophylactic aspirin protocols. The study was approved by the HFH Institutional Review Board (IRB #14558). Patients were considered at high risk for preeclampsia if they met one or more high-risk criteria as defined in the ACOG practice bulletin.[1] Exclusion criteria included pregnancies with major fetal abnormalities, patients who were receiving aspirin prior to pregnancy, and patients with von Willebrand disease, peptic ulcers, hypersensitivity to aspirin, long-term use of nonsteroidal anti-inflammatory medication, or coronavirus disease 2019.

Patients were divided into three groups. Those cared for from January 2013 through September 2015 were treated before an aspirin protocol for preeclampsia prophylaxis had been established (no aspirin group). Patients cared for from October 2015 through January 2019 were treated under a standard protocol for preeclampsia prophylaxis of daily aspirin at 81 mg from 12 weeks of pregnancy until delivery (81 mg group). Patients cared for from February 2019 through December 2020 were treated under an increased daily aspirin dose protocol for preeclampsia prophylaxis at 162 mg from 12 weeks of pregnancy until delivery (162 mg group). Only patients who delivered after 20 weeks of gestation within those time periods were included.

Data were extracted from the EPIC electronic medical record at HFH. Demographic information, health characteristics, and current and past features of pregnancy were extracted. Patient race was extracted as had been self-reported in the medical record, and because most patients were either black/African American or white, all other races were combined into an "other" designation. Primary outcome was preeclampsia diagnosed at any time throughout pregnancy. Secondary outcomes were fetal growth restriction, birth weight, preterm birth, gestational hypertension, peripartum cardiomyopathy, pulmonary edema, placental abruption, fetal death, neonatal death, and admission to the neonatal intensive care unit (NICU). Maternal and fetal clinical features and effects traditionally associated with aspirin use were assessed, including postpartum hemorrhage, postpartum hematoma, thrombocytopenia, anesthetic complications, transaminitis, hematuria in urine, and renal failure for patients, and necrotizing enterocolitis and neonatal intraventricular hemorrhage for newborns.

Statistical Analysis

Groups were compared with analysis of variance, two-sample *t*-test, Kruskal–Wallis test, or Wilcoxon tank sum test, as indicated. Categorical data were analyzed with chi-square or Fisher's exact tests based on expected cell counts. Multivariable logistic regression models were used to adjust for baseline variables. Moderate and high-risk factors for preeclampsia were included in the regression model. Odds ratios (ORs) and adjusted ORs (aORs) were calculated for the regression models with 95% confidence intervals (95% CIs). Continuous variables were calculated as mean ± standard deviation. Categorical variables were calculated as counts and percentages. Rates of preeclampsia and secondary maternal and fetal outcomes were compared between groups. When significant differences were observed, pairwise testing was performed applying a Benjamini–Hochberg correction to control for multiple comparisons. Continuous data were evaluated for normality using QQ plots, histograms, and Shapiro–Wilk tests.

Table 1 Demographic and clinical characteristics of patients at risk for preeclampsia

Characteristics	Aspirin dose ($N = 3,597$)			*p*-Value	
	No aspirin ($n = 2,266$)	81 mg ($n = 944$)	162 mg ($n = 387$)	All groups	81 vs. 162 mg
Maternal age at delivery (y)	30.1 ± 5.8	30.6 ± 5.8	31.2 ± 6.3	**0.002 (A)**	0.119 (T)
Race					
Black	734 (32.4)	531 (56.3)	177 (45.7)	**<0.001 (C)**	**0.001 (C)**
White	1,134 (50.0)	298 (31.6)	145 (37.5)		
Other	351 (15.5)	104 (11.0)	61 (15.8)		
Gravida	3.4 ± 2.1	3.5 ± 2.3	3.4 ± 2.4	0.642 (KW)	0.392 (W)
Parity	1.5 ± 1.5	1.5 ± 1.5	1.5 ± 1.7	0.154 (KW)	0.268 (W)
Smoking	110 (4.9)	68 (7.2)	43 (11.1)	0.059 (C)	0.117 (C)
Illicit drug use	64 (2.8)	46 (4.9)	31 (8.0)	**<0.001 (C)**	**0.029 (C)**
History of gestational diabetes	890 (39.3)	409 (43.3)	148 (38.2)	0.072 (C)	0.088 (C)
History of gestational hypertension	571 (25.2)	539 (57.1)	247 (63.8)	**<0.001 (C)**	**0.023 (C)**
History of preterm birth	61 (2.7)	53 (5.6)	15 (3.9)	**<0.001 (C)**	0.191 (C)

Notes: Data shown as *n* (%) or mean ± standard deviation. A, analysis of variance; T, two-sample *t*-test; C, chi-square test; KW, Kruskal–Wallis test; W, Wilcoxon rank sum test. Significance is defined at $p < 0.05$. All significant values are displayed in bold.

Statistical significance was set at $p < 0.05$, and all tests were two-sided.

Sample Size and Power Analysis

Assuming a rate of preeclampsia of 8% in the no aspirin group, 6% in the 81 mg group, and 3% in the 162 mg group, an average proportion of 5.7% and a variance of proportions of < 0.001 would be detectable with a sample size of 407 in each group using a 0.05-level chi-square test. A target sample size of 1,221 with equal-sized groups was planned.

Results

Of the 3,597 patients included in the study, 2,266 patients (63%) were in the no aspirin group, 944 (26%) were in the 81 mg group, and 387 (11%) were in the 162 mg group. ►Table 1 shows patient characteristics for all groups. The no aspirin group included a higher proportion of patients who were white and a lower proportion of patients with a history of gestational hypertension than the two aspirin groups. ►Table 2 outlines the preeclampsia risk factors for

Table 2 Preeclampsia risk factors

Risk factors	Aspirin dose *n* (%) ($N = 3,597$)			*p*-Value[a]	
	No aspirin ($n = 2,266$)	81 mg ($n = 944$)	162 mg ($n = 387$)	All groups	81 vs. 162 mg
History of preeclampsia	889 (39.2)	270 (28.6)	77 (19.9)	**<0.001**	**0.001**
Multifetal gestation	253 (11.6)	142 (15.0)	46 (11.9)	**0.018**	0.155
Renal disease	200 (8.8)	51 (5.4)	19 (4.9)	**<0.001**	0.714
Autoimmune disease	5 (0.2)	57 (6.0)	31 (8.0)	**<0.001**	0.189
Type 1 diabetes	605 (26.7)	231 (24.5)	90 (23.3)	0.209	0.638
Type 2 diabetes	605 (26.7)	256 (27.1)	113 (29.2)	0.592	0.441
Chronic hypertension	711 (31.4)	571 (60.5)	249 (64.3)	**<0.001**	0.189
First pregnancy	562 (25.9)	270 (28.7)	125 (32.4)	**0.016**	0.182
Age ≥ 35 years	522 (23.0)	243 (25.7)	112 (28.9)	**0.023**	0.231
BMI ≥ 30 kg/m^2	590 (26.0)	490 (51.9)	172 (44.4)	**<0.001**	**0.013**
Black race	734 (33.1)	531 (56.9)	177 (46.2)	**<0.001**	**<0.001**
History of low birth weight	161 (7.1)	33 (3.5)	6 (1.6)	**<0.001**	0.056
10-year pregnancy interval	54 (2.4)	56 (5.9)	27 (7.0)	**<0.001**	0.474

Abbreviation: BMI, body mass index.
Note: Significance is defined at $p < 0.05$. All significant values are displayed in bold.
[a]Chi-square test was used to calculate *p*-values.

patients in each group. The no aspirin group included a higher proportion of patients with a history of preeclampsia, but lower proportions of black patients and patients with chronic hypertension or obesity (body mass index [BMI] $\geq$ 30 kg/m^2) than the two aspirin groups.

The rate of preeclampsia was significantly lower in the 162 mg group (10.1%, OR, 0.68; 95% CI, 0.46–0.99) compared with the 81 mg group (14.2%; ►Table 3). Also, 322 patients (14.2%) in the no aspirin group developed preeclampsia, which was the same rate as the 81 mg group. Analysis of secondary outcomes showed that several outcomes differed significantly between the three groups, revealing that the no aspirin group had the lowest rates of preterm birth and current gestational hypertension. Also, patients in the no aspirin group had the lowest rate of fetal growth restriction. However, two-way comparisons showed no significant differences for any secondary outcomes between the 81 and 162 mg groups except for admission to the NICU. The rate of NICU admission was significantly lower in the 162 mg group (22.1%, OR, 0.75; 95% CI, 0.57–0.97) compared with the 81 mg group (27.6%; ►Table 3). After adjusting for baseline characteristics (black race, illicit drug use, history of gestational hypertension, history of prior preeclampsia, and BMI $\geq$ 30), the odds of developing preeclampsia remained significantly lower in the 162 mg group compared with the 81 mg group (aOR, 0.61; 95% CI, 0.39–0.97); however, the odds of admission to the NICU were no longer statistically significant (►Table 3).

Assessment of clinical features and side effects traditionally associated with the use aspirin revealed no significant differences between the 81 and 162 mg groups for postpartum hemorrhage, postpartum hematoma, thrombocytopenia, transaminitis, renal failure, or intraventricular hemorrhage of the newborn (►Table 4). However, analysis that included all three groups showed that women in the no aspirin group had the lowest rate of postpartum hemorrhage and thrombocytopenia, the highest rate of renal failure, and had newborns with the lowest rate of intraventricular hemorrhage (►Table 4).

Discussion

In this retrospective cohort study, we observed that patients who were at high risk for preeclampsia and were treated under a 162 mg prophylactic aspirin protocol had a significantly lower rate of preeclampsia than women who received the standard 81 mg dose regimen alongside no apparent increased risk for bleeding. Of note, the rates of preeclampsia in our patient population were 10 to 14%, which is higher than that reported for the general population at 2 to 8%.[2,3] This might be attributed to features of a unique population within the metro-Detroit community, who may have higher barriers to care and more social determinants of health; all of which ultimately create a higher risk community at baseline.

To our knowledge, no previous studies have evaluated aspirin at 162 mg dosing for preeclampsia prevention, although many have evaluated the benefits of aspirin prophylaxis at different dosages, gestational age of prophylaxis initiation, and preeclampsia risk definitions, as well as within populations with variable risk profiles.[12] Previous studies have also shown conflicting outcomes as to the role of aspirin in preeclampsia prevention. For example, in 1994, the CLASP study (Collaborative Low-dose Aspirin Study in Pregnancy) was one of the original and largest randomized controlled trials to assess the efficacy and safety of aspirin for preventing preeclampsia in at-risk pregnant patients, concluding that in over 9,000 subjects, low-dose aspirin was generally safe for the fetus and newborn, with no evidence of an increased likelihood of maternal or fetal bleeding.[15,16] However, this trial also concluded that a daily dosage of aspirin at 60 mg did not lead to a reduction in preeclampsia rates and showed that patients at a lower gestational age had lower rates of preeclampsia.[15,16] In 2007, a large meta-analysis reported an approximate 10% risk reduction for the incidence of preeclampsia in women treated with antiplatelet therapy.[12] The meta-analysis included studies that used 15 different definitions for preeclampsia, and the doses of aspirin ranged from 50 to 150 mg, with some of the studies having started the aspirin prophylaxis after 20 weeks of gestation.[12] Subsequent meta-analyses showed the effectiveness of aspirin in reducing preeclampsia rates if initiated prior to 16 weeks of gestational age.[17–19] The effect of aspirin was also previously thought to be dose-dependent with maximal effect noted at daily doses of over 100 mg. But these studies have been criticized because they used aggregate data and hence could have overestimated the effect size of aspirin.[20] Compared with our current study, the aforementioned studies were randomized control trials or meta-analyses that presented conflicting evidence regarding the role of aspirin for preeclampsia prevention, and importantly they did not include doses at 162 mg.

The highest dose of aspirin studied thus far in the literature is 150 mg, and this dose represents the formulation compatible with many European countries. In 2017, the ASPRE clinical trial (Aspirin for Evidence-Based Preeclampsia Prevention) was done to look at the role of 150 mg aspirin on reduction of preeclampsia rates.[21,22] This blinded study showed a reduction in the incidence of preterm preeclampsia for patients who were randomly allocated to receive 150 mg.[21] A secondary analysis of the ASPRE data revealed a consistent effect size for prophylactic aspirin within subgroups according to recognized risk factors for preeclampsia,[23] and another secondary analysis also showed a reduction in NICU length of stay in the NICU.[24] While our study was a retrospective study and did not assess NICU length of stay, our study showed a significantly lower rate of NICU admissions in neonates born to mothers receiving aspirin at 162 mg compared with 81 mg. However, when adjusted for baseline variables, the lower rate of NICU admissions was no longer significant.

Regarding the safety profile of aspirin, a recent systematic review from the USPSTF showed that low-dose aspirin use, ranging between 50 and 150 mg, was not associated with maternal or neonatal harm within the normal follow-up through an 18-year period.[4] Other studies have shown no association between the use of aspirin in pregnancy and

Table 3 Univariate and multivariable associations of different doses of prophylactic aspirin with maternal and neonatal outcomes

Outcomes	Aspirin dose *n* (%)			*p*-Value		OR (95% CI)	aOR[a] (95% CI)
	No aspirin (*n* = 2,266)	81 mg (*n* = 944)	162 mg (*n* = 387)	All groups	81 vs. 162 mg	81 vs. 162 mg	81 vs. 162 mg
Primary outcome in patients (*N* = 3,597)							
Preeclampsia	322 (14.2)	134 (14.2)	39 (10.1)	0.084 (C)	**0.043 (C)**	**0.68 (0.46–0.99)**	**0.61 (0.39–0.97)**
Secondary outcomes in patients (*N* = 3,597)							
Preterm birth	463 (20.4)	325 (34.4)	116 (30.0)	**<0.001 (C)**	0.117 (C)	0.82 (0.63–1.05)	0.77 (0.55–1.07)
Current gestational hypertension	324 (14.3)	183 (19.4)	70 (18.1)	**<0.001 (C)**	0.584 (C)	0.92 (0.68–1.25)	0.82 (0.55–1.23)
Peripartum cardiomyopathy	6 (0.3)	8 (0.8)	1 (0.3)	0.075 (F)	0.461 (F)	0.30 (0.04–2.43)	–
Pulmonary edema	0 (0.0)	6 (0.6)	0 (0.0)	**<0.001 (F)**	0.190 (F)	–	–
Placental abruption	43 (1.9)	27 (2.9)	9 (2.3)	0.234 (C)	0.585 (C)	0.81 (0.38–1.74)	1.04 (0.43–2.56)
Secondary outcomes in neonates (*N* = 4,034)							
	No aspirin (*n* = 2,513)	81-mg (*n* = 1,087)	162-mg (*n* = 434)	All groups	81- vs. 162-mg	81 vs. 162 mg	81 vs. 162 mg
Birth weight (≥3,000 g)	1,460 (58.4)	424 (39.0)	185 (42.7)	**<0.001 (A)**	0.583 (T)	1.16 (0.93–1.46)	1.20 (0.90–1.61)
Fetal growth restriction	453 (18.0)	266 (24.5)	101 (23.3)	**<0.001 (C)**	0.622 (C)	0.94 (0.72–1.22)	0.98 (0.71–1.34)
Fetal death	24 (1.0)	9 (0.8)	6 (1.4)	0.605 (C)	0.388 (F)	1.68 (0.59–4.75)	–
Neonatal death	12 (0.5)	6 (0.6)	3 (0.7)	0.896 (C)	0.721 (F)	1.25 (0.31–5.01)	–
NICU Admission	377 (15.0)	300 (27.6)	96 (22.1)	**<0.001 (C)**	**0.028 (C)**	**0.75 (0.57–0.97)**	0.84 (0.60–1.17)

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; NICU, neonatal intensive care unit; OR, odds ratio.
Note: Significance is defined at $p < 0.05$. All significant values are displayed in bold. Data shown as *n* (%) or mean ± standard deviation. C, chi-square test; A, analysis of variance; T, two-sample *t*-test; F, Fisher's exact test.
[a]Adjusted for: AA race, illicit drug use, history of gestational hypertension, history of prior preeclampsia, and BMI ≥ 30.

Table 4 Univariate and multivariable associations of different doses of prophylactic aspirin with bleeding complications

	Aspirin dose *n* (%)			*p*-Value		OR (95% CI)	aOR[a] (95% CI)
	No aspirin ($n=2,266$)	81 mg ($n=944$)	162 mg ($n=387$)	All groups	81 vs. 162 mg	81 vs. 162 mg	81 vs. 162 mg
Patients ($N=3,597$)							
Postpartum hemorrhage	108 (4.8%)	59 (6.3%)	31 (8.0%)	**0.018 (C)**	0.245 (C)	1.31 (0.83–2.05)	1.20 (0.69–2.11)
Postpartum hematoma	4 (0.2%)	0 (0.0%)	0 (0.0%)	–	–	–	–
Thrombocytopenia	81 (3.6%)	76 (8.1%)	24 (6.2%)	**<0.001 (C)**	0.245 (C)	0.76 (0.47–1.21)	0.79 (0.43–1.44)
Anesthetic complications	9 (0.4%)	2 (0.2%)	1 (0.3%)	0.824 (F)	> 0.99 (F)	1.22 (0.11–13.50)	–
Transaminitis	8 (0.4%)	5 (0.5%)	2 (0.5%)	0.669 (F)	> 0.99 (F)	0.98 (0.19–5.05)	–
Hematuria in urine	45 (2.0%)	28 (3.0%)	10 (2.6%)	0.225 (C)	0.704 (C)	0.87 (0.42–1.80)	0.54 (0.21–1.35)
Renal failure	198 (8.7%)	43 (4.6%)	12 (3.1%)	**<0.001 (C)**	0.226 (C)	0.67 (0.35–1.29)	0.66 (0.29–1.50)
Neonates ($N=4,034$)	No aspirin ($n=2,513$)	81 mg ($n=1,087$)	162 mg ($n=434$)	All groups	81 vs. 162 mg	81 vs. 162 mg	81 vs. 162 mg
Necrotizing enterocolitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	–	–	–	–
Neonatal intraventricular hemorrhage	33 (1.3%)	32 (2.9%)	8 (1.8%)	**0.003 (C)**	0.226 (C)	0.62 (0.28–1.35)	0.39 (0.13–1.13)

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; OR, odds ratio.

Note: Significance is defined at $p<0.05$. All significant values are displayed in bold. C, chi-square test; F, Fisher's exact test. Three-way comparisons were done with analysis of variance (ANOVA); two-way comparisons were done with chi-square test.

[a]Adjusted for: AA race, illicit drug use, history of gestational hypertension, history of prior preeclampsia, and BMI $\geq$ 30.

neonatal outcomes such as intraventricular hemorrhage, neonatal bleeding, or antenatal closure of the ductus arteriosus, nor any association with maternal outcomes such as major postpartum bleeding, placental abruption, or adverse regional anesthetic outcomes.[25–29] With that said, a recent study from Sweden showed conflicting results regarding the safety of aspirin during pregnancy, concluding that aspirin use, specifically at 75 mg dosing, was associated with increased postpartum bleeding and postpartum hematoma as well as with neonatal intracranial hemorrhage.[30] Our study supports earlier findings regarding the safety of using aspirin at 162 mg dosing, revealing no significant differences between higher and lower doses in terms of postpartum bleeding, hematomas, neonatal intracranial hemorrhage, and other adverse effects.

Strengths and Limitations

Our study suggests that recommending aspirin prophylaxis at 162 mg for patients at high risk for preeclampsia may be clinically relevant, and controlled clinical trials of this specific regimen are needed. Current ACOG and SMFM guidelines recommend aspirin at 81 mg for preeclampsia prophylaxis; however, patients in our study who received this standard regimen had the same rate of preeclampsia as those who did not take prophylactic aspirin at all. Given that this is the first study to investigate the association of 162 mg dosing of aspirin with preeclampsia and birth outcomes, other studies with different patient distributions and within different settings will be needed. The strengths of this study include a large sample size, detailed descriptions of baseline characteristics and preeclampsia risk factors for three study groups, and examination of a large number of secondary outcomes.

Limitations of this study include the retrospective nature and potential for selection bias, misclassification bias, and missing data. Given that the data were obtained via a computer-generated software tool, misclassification bias due to incomplete medical records or errors in disease or risk factors coding were possible.

Conclusion

In conclusion, our study demonstrated that a higher dose of aspirin at 162 mg for preeclampsia prophylaxis in patients at high risk for this complication was associated with a lower rate of preeclampsia than in patients who took the standard dose at 81 mg. We recommend considering the implementation of aspirin 162 mg dosing for preeclampsia prophylaxis in patients with high-risk features and hope that further studies will refine our understanding of how aspirin can help prevent this serious complication of pregnancy.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

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None.

Conflict of Interest

None declared

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