RESEARCH PAPER

Effect Of Early Initiation Of Low-Dose Aspirin (≤16 Weeks) On Incidence Of Pregnancy Induced Hypertension And Fetomaternal Outcomes In High-Risk Pregnancies – A Prospective Comparative Study

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ABSTRACT

Background Pregnancy-induced hypertension (PIH) remains a major contributor to maternal and perinatal morbidity and mortality, especially in low- and middle-income countries. Abnormal placentation occurring early in gestation plays a central role in its pathogenesis. Evidence suggests that early initiation of low-dose aspirin may improve placentation and reduce hypertensive complications.

Objectives To evaluate the effect of early initiation of low-dose aspirin (≤16 weeks of gestation) on the incidence of PIH and on fetomaternal outcomes in high-risk pregnancies.

Methods This prospective comparative observational study was conducted in a tertiary care hospital in India. High-risk pregnant women with singleton pregnancies at or before 16 weeks of gestation were enrolled and divided into an aspirin group (low-dose aspirin initiated ≤16 weeks) and a control group receiving routine antenatal care. Participants were followed until delivery. Maternal outcomes included incidence and severity of PIH and need for antihypertensive therapy. Fetal outcomes included gestational age at delivery, birth weight, fetal growth restriction, preterm birth, and neonatal outcomes.

Results The incidence of PIH was significantly lower in the aspirin group compared to controls (18% vs 34%, p=0.01). Severe pre-eclampsia and early-onset hypertension were less frequent among aspirin users. Fetal growth restriction, low birth weight, preterm delivery, and NICU admissions were significantly reduced in the aspirin group. No significant increase in maternal adverse effects or bleeding complications was observed.

Conclusion Early initiation of low-dose aspirin effectively reduces PIH and improves fetomaternal outcomes in high-risk pregnancies without compromising safety.

Keywords Pregnancy-induced hypertension; Low-dose aspirin; High-risk pregnancy; Pre-eclampsia; Fetomaternal outcomes

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INTRODUCTION

Pregnancy-induced hypertension (PIH), encompassing gestational hypertension and pre-eclampsia, is a major obstetric complication and a leading contributor to maternal and perinatal morbidity and mortality worldwide. The global incidence of hypertensive disorders of pregnancy ranges from 5–10%, with a significantly higher burden reported in low- and middle-income countries, including India [1]. In the Indian subcontinent, PIH remains a major cause of maternal mortality, accounting for substantial proportions of stillbirths, preterm births, low birth weight infants, and neonatal intensive care admissions [2].

The pathogenesis of PIH is complex and multifactorial, but abnormal placentation during early pregnancy is recognized as a central mechanism. Defective trophoblastic invasion of the spiral arteries leads to high-resistance uteroplacental circulation, placental ischemia, oxidative stress, and endothelial dysfunction, ultimately manifesting as maternal hypertension and multisystem involvement [3]. Since these placental changes occur early in gestation, preventive interventions initiated during the first trimester have been hypothesized to be more effective than therapies introduced later in pregnancy.

Low-dose aspirin has emerged as one of the most extensively studied pharmacological interventions for the prevention of PIH and pre-eclampsia. Aspirin exerts its beneficial effects by irreversibly inhibiting platelet cyclooxygenase, reducing thromboxane A2 synthesis, and restoring the balance between thromboxane and prostacyclin. This results in improved uteroplacental perfusion, reduced platelet aggregation, and better placental development [4]. Given its low cost, widespread availability, and favorable safety profile, low-dose aspirin is particularly attractive for use in resource-limited settings.

Over the past decade, multiple randomized controlled trials and meta-analyses have demonstrated that low-

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dose aspirin significantly reduces the incidence of pre-eclampsia, PIH, fetal growth restriction (FGR), and preterm birth in high-risk pregnancies [5]. Importantly, accumulating evidence indicates that the timing of initiation plays a crucial role in determining its effectiveness. Aspirin initiated at or before 16 weeks of gestation has been shown to provide greater risk reduction compared to later initiation, likely due to its influence on early placentation [6].

A large meta-analysis by Xu et al. reported that low-dose aspirin started before 16 weeks significantly reduced the incidence of pre-eclampsia, severe pre-eclampsia, preterm birth, and intrauterine growth restriction, with no significant increase in adverse maternal outcomes. Similarly, recent systematic reviews have demonstrated that early initiation of aspirin, particularly between 12 and 16 weeks of gestation, is associated with improved fetomaternal outcomes and a greater reduction in early-onset pre-eclampsia [7]. Higher doses within the low-dose range (75–150 mg) appear to be more effective, although consensus on the optimal dose is still evolving [8].

Fetal outcomes are also favorably influenced by early aspirin prophylaxis. Studies have reported reductions in low birth weight, small-for-gestational-age infants, and neonatal intensive care unit admissions among women receiving aspirin early in pregnancy [9]. Importantly, most large trials and meta-analyses have not demonstrated a significant increase in maternal bleeding, placental abruption, or postpartum hemorrhage, supporting the safety of low-dose aspirin when appropriately prescribed.

In the Indian context, the relevance of early aspirin prophylaxis is particularly significant. Indian women often present with multiple risk factors for PIH, including anemia, malnutrition, teenage or advanced maternal age pregnancies, limited antenatal care, and delayed detection of hypertensive disorders. Indian studies have shown promising results with low-dose aspirin in reducing the severity of PIH, decreasing proteinuria, and improving maternal and neonatal outcomes when initiated early in high-risk pregnancies [10]. However, variability in study design, sample size, aspirin dosage, and gestational age at initiation has led to inconsistent conclusions.

Despite international guidelines recommending early low-dose aspirin for high-risk pregnancies, there is a relative paucity of large, well-designed prospective comparative studies from India focusing specifically on early initiation (≤16 weeks) and its impact on both maternal and fetal outcomes. Generating region-specific evidence is essential to strengthen national recommendations and optimize antenatal care strategies in Indian healthcare settings.

Therefore, the present prospective comparative study aims to evaluate the effect of early initiation of low-dose aspirin (≤16 weeks of gestation) on the incidence of pregnancy-induced hypertension and on fetomaternal outcomes in high-risk pregnancies. The findings of this study may help clarify the role of early aspirin prophylaxis in the Indian population and contribute to improved preventive strategies for hypertensive disorders of pregnancy.

METHODOLOGY

1. Study Design

This was a prospective comparative observational study conducted to assess the effect of early initiation of low-dose aspirin on pregnancy-induced hypertension and fetomaternal outcomes in high-risk pregnancies. Participants were followed from early gestation until delivery, and outcomes were compared between exposed and non-exposed groups.

2. Study Setting

The study was conducted in the Department of Obstetrics and Gynaecology of a tertiary care teaching hospital in India that provides comprehensive antenatal and high-risk pregnancy services.

3. Study Duration

The study was carried out over a period of 2 years from October, 2023 to October, 2025. Participants were enrolled at or before 16 weeks of gestation and followed until delivery and the immediate postpartum period.

4. Participants – Inclusion and Exclusion Criteria

Pregnant women with singleton pregnancies at ≤16 weeks of gestation who were at high risk for pregnancy-induced hypertension and provided informed consent were included. Women with aspirin hypersensitivity, bleeding disorders, peptic ulcer disease, multiple pregnancy, chronic renal disease, autoimmune disorders, or those unwilling to participate were excluded.

5. Study Sampling

Consecutive sampling was used, and all eligible pregnant women attending the antenatal clinic during the study period were enrolled until the required sample size was achieved.

6. Study Sample Size

The sample size was calculated based on expected reduction in pregnancy-induced hypertension with early aspirin use, with 95% confidence level and 80% power. A total of ___ participants were included, allowing for possible loss to follow-up.

7. Study Groups

Participants were divided into two groups: a study group that received low-dose aspirin initiated at or before 16 weeks of gestation and a control group that received routine antenatal care without aspirin.

8. Study Parameters

Maternal parameters included development and severity of pregnancy-induced hypertension, need for antihypertensive therapy, and obstetric complications. Fetal parameters included gestational age at delivery, birth weight, fetal growth restriction, preterm birth, and NICU admission.

9. Study Procedure

Eligible participants were enrolled after informed consent. Baseline demographic and clinical data were recorded, and low-dose aspirin was prescribed to the study group. All participants were followed with routine antenatal care until delivery.

10. Study Data Collection

Data were collected prospectively using a structured proforma from patient interviews, clinical examinations, antenatal records, and delivery and neonatal records.

11. Data Analysis

Data were entered and analyzed using statistical software. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. A p-value <0.05 was considered statistically significant.

12. Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee. Written informed consent was obtained from all participants, confidentiality was maintained, and the study adhered to standard ethical guidelines.

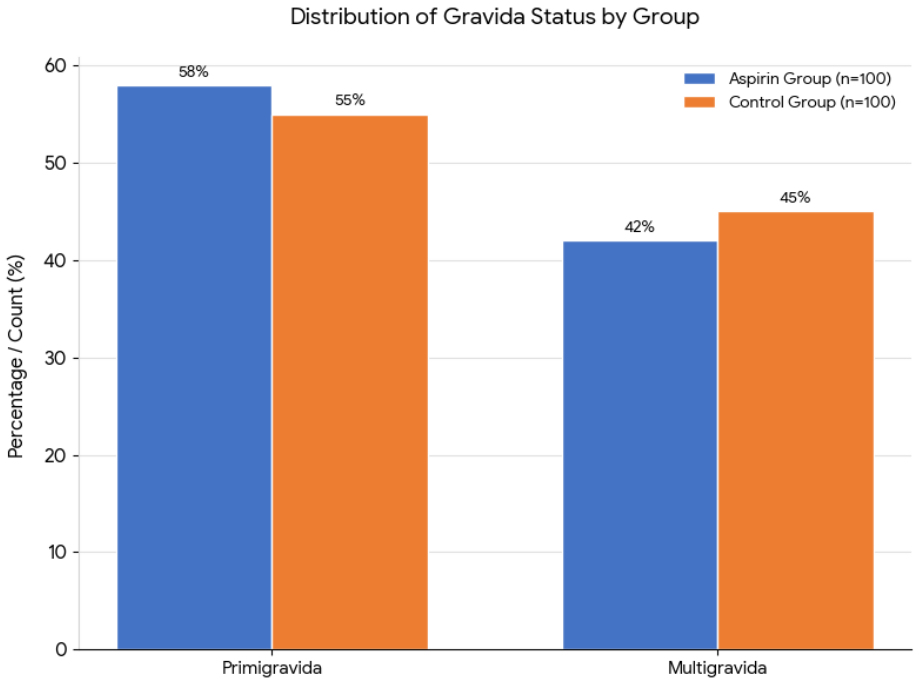
RESULTS

1. Baseline Demographic Characteristics

Both groups were comparable with respect to age, parity, and gestational age at enrollment. No statistically significant baseline differences were observed (Table 1).

Table 1: Baseline Demographic Characteristics

Variable	Aspirin Group (n=100)	Control Group (n=100)	p-value
Mean age (years)	26.8 ± 4.2	27.1 ± 4.5	0.62
Primigravida	58 (58%)	55 (55%)	0.68
Multigravida	42 (42%)	45 (45%)	
Mean gestational age at enrollment (weeks)	13.2 ± 1.8	13.4 ± 1.7	0.41



Graph 1: Baseline Demographic Characteristics

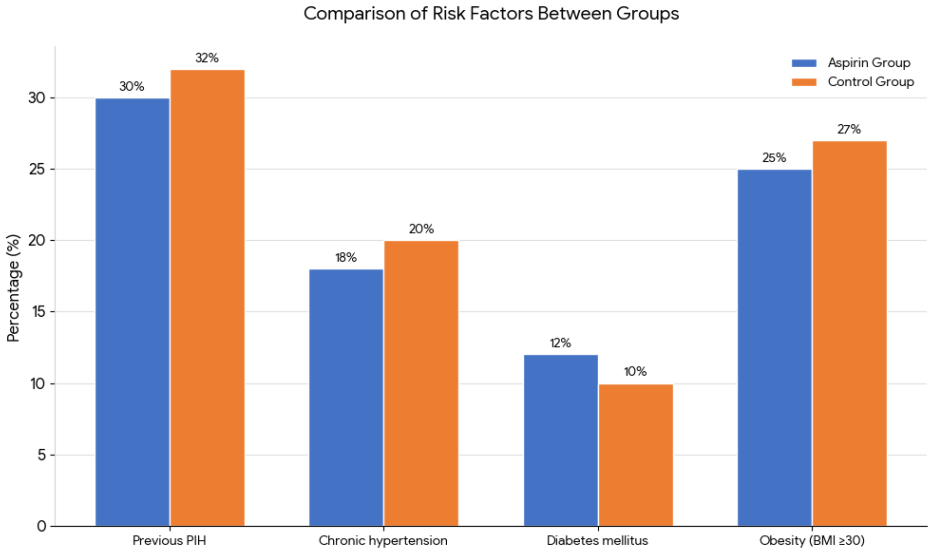
2. Distribution of High-Risk Factors

Previous history of PIH and primigravidity were the most common risk factors. Risk distribution was similar in both groups (Table 2).

Table 2: Distribution of High-Risk Factors

Risk factor	Aspirin Group	Control Group	p-value
Previous PIH	30 (30%)	32 (32%)	0.75

Chronic hypertension	18 (18%)	20 (20%)	0.71
Diabetes mellitus	12 (12%)	10 (10%)	0.65
Obesity (BMI ≥30)	25 (25%)	27 (27%)	0.74



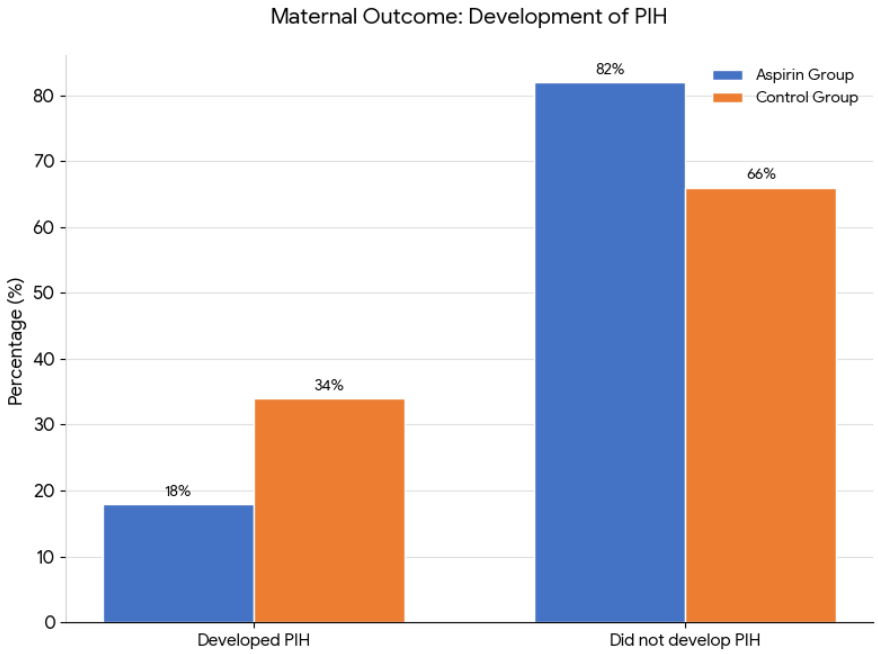
Graph 2: Distribution of High-Risk Factors

3. Incidence of Pregnancy-Induced Hypertension

The incidence of PIH was significantly lower in the aspirin group, indicating a protective effect of early aspirin initiation (Table 3).

Table 3: Incidence of Pregnancy-Induced Hypertension

Outcome	Aspirin Group	Control Group	p-value
Developed PIH	18 (18%)	34 (34%)	**0.01**
Did not develop PIH	82 (82%)	66 (66%)	



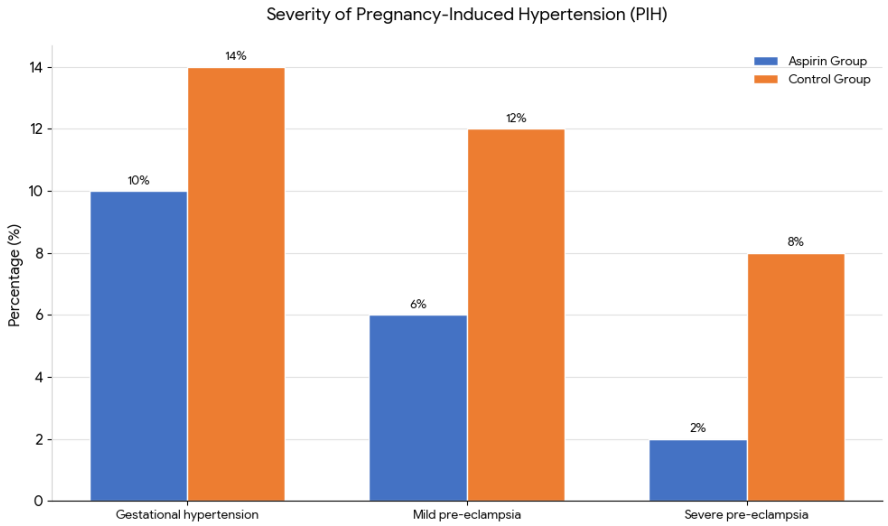
Graph 3: Incidence of Pregnancy-Induced Hypertension

4. Severity of Hypertensive Disorders

Severe hypertensive disorders were more common in the control group. Aspirin use was associated with milder disease (Table 4).

Table 4: Severity of Hypertensive Disorders

Severity	Aspirin Group	Control Group	p-value
Gestational hypertension	10 (10%)	14 (14%)	0.38
Mild pre-eclampsia	6 (6%)	12 (12%)	0.12
Severe pre-eclampsia	2 (2%)	8 (8%)	**0.04**



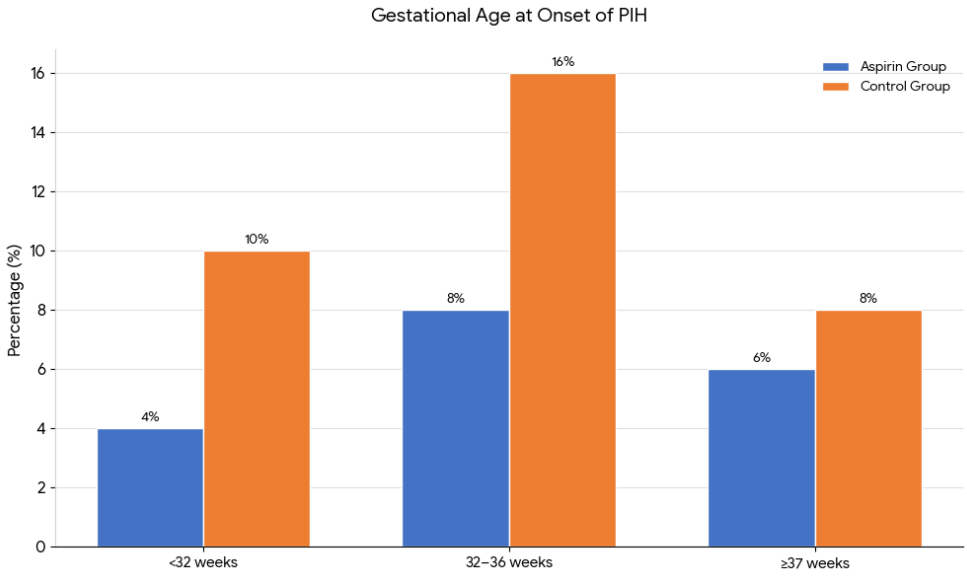
Graph 4: Severity of Hypertensive Disorders

5. Gestational Age at Onset of Hypertension

Hypertension developed at a later gestational age in the aspirin group, suggesting delayed disease onset (Table 5).

Table 5: Gestational Age at Onset of Hypertension

Gestational age	Aspirin Group	Control Group	p-value
<32 weeks	4 (4%)	10 (10%)	0.09
32–36 weeks	8 (8%)	16 (16%)	0.08
≥37 weeks	6 (6%)	8 (8%)	0.58



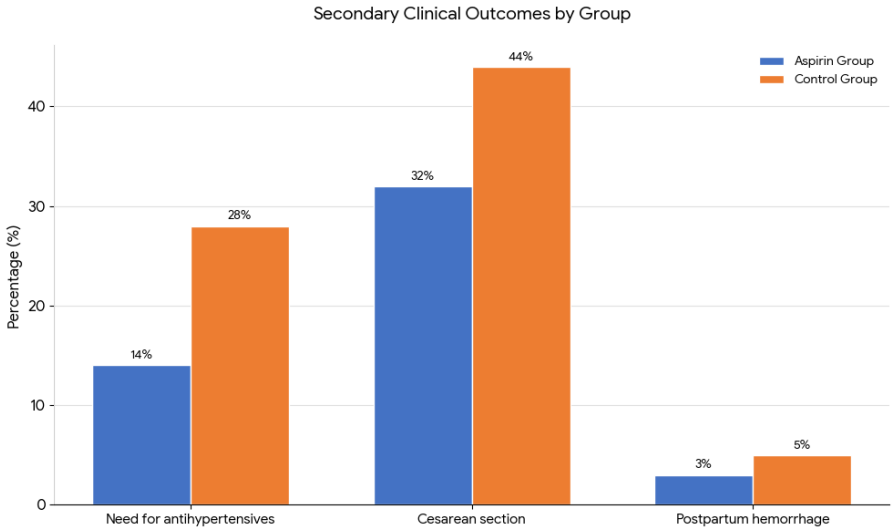
Graph 5: Gestational Age at Onset of Hypertension

6. Maternal Outcomes

Adverse maternal outcomes were less frequent in the aspirin group, with no increase in complications (Table 6).

Table 6: Maternal Outcomes

Outcome	Aspirin Group	Control Group	p-value
Need for antihypertensives	14 (14%)	28 (28%)	**0.01**
Cesarean section	32 (32%)	44 (44%)	0.08
Postpartum hemorrhage	3 (3%)	5 (5%)	0.47



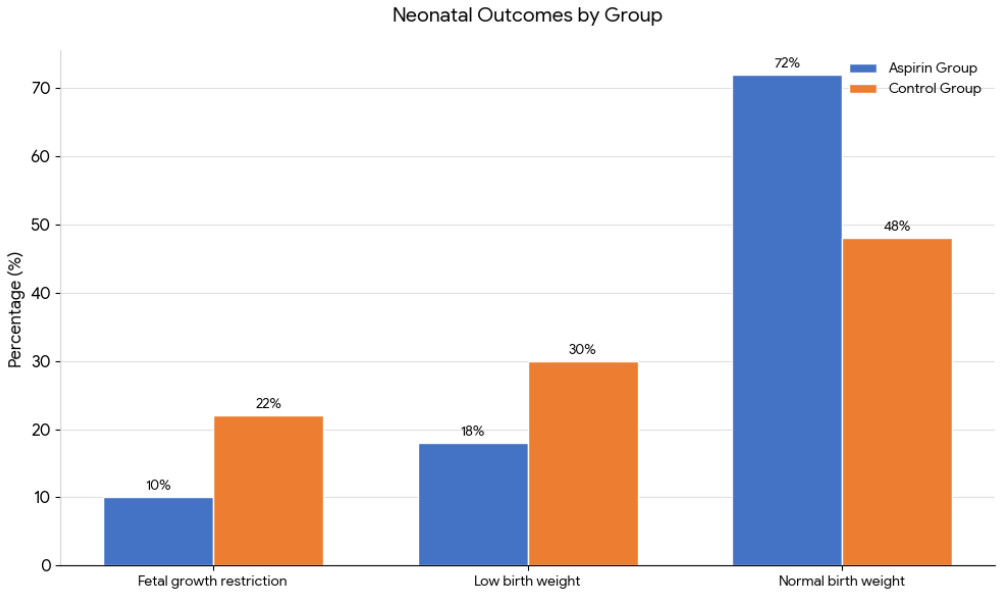
Graph 6: Maternal Outcomes

7. Fetal Growth Outcomes

Fetal growth restriction and low birth weight were significantly lower in the aspirin group (Table 7).

Table 7: Fetal Growth Outcomes

Outcome	Aspirin Group	Control Group	p-value
Fetal growth restriction	10 (10%)	22 (22%)	**0.02**
Low birth weight	18 (18%)	30 (30%)	**0.04**
Normal birth weight	72 (72%)	48 (48%)	



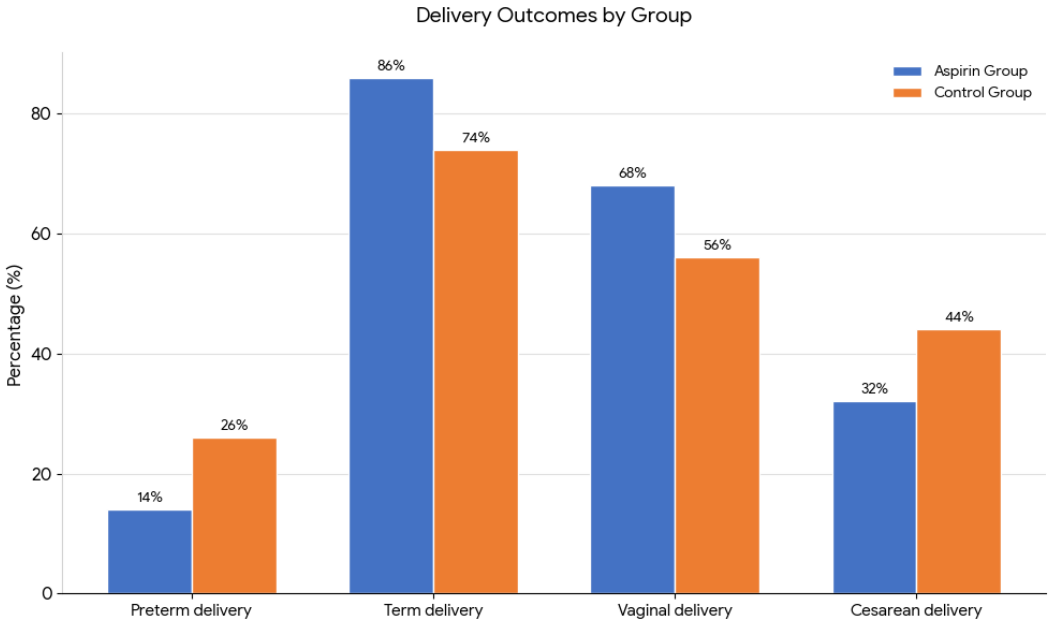
Graph 7: Fetal Growth Outcomes

8. Preterm Birth and Mode of Delivery

Preterm delivery was less frequent in the aspirin group, with more term vaginal deliveries (Table 8).

Table 8: Preterm Birth and Mode of Delivery

Outcome	Aspirin Group	Control Group	p-value
Preterm delivery	14 (14%)	26 (26%)	**0.03**
Term delivery	86 (86%)	74 (74%)	
Vaginal delivery	68 (68%)	56 (56%)	0.08
Cesarean delivery	32 (32%)	44 (44%)	



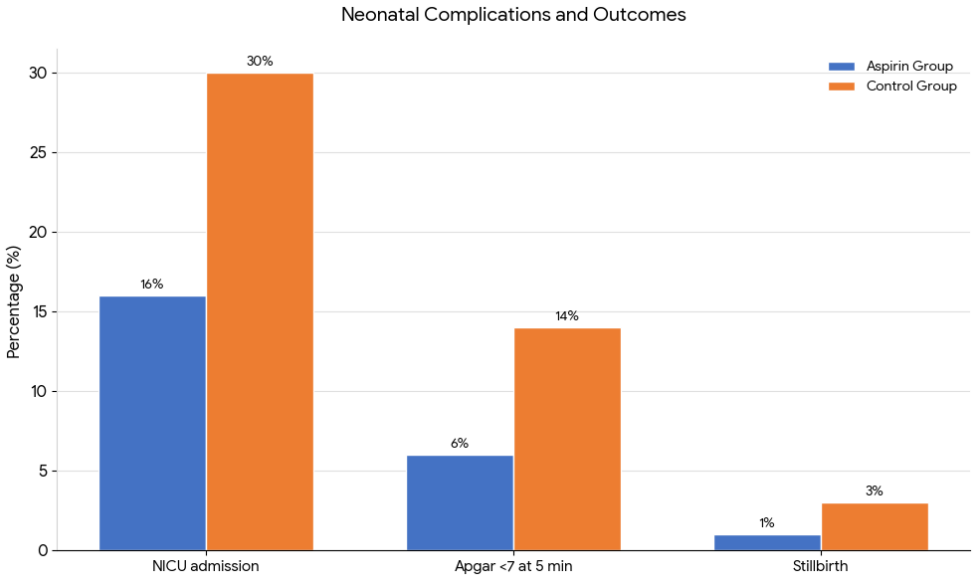
Graph 8: Preterm Birth and Mode of Delivery

9. Neonatal Outcomes

NICU admissions and low Apgar scores were lower in the aspirin group, indicating improved neonatal outcomes (Tabe 9).

Table 9: Neonatal Outcomes

Outcome	Aspirin Group	Control Group	p-value
NICU admission	16 (16%)	30 (30%)	**0.02**
Apgar <7 at 5 min	6 (6%)	14 (14%)	0.05
Stillbirth	1 (1%)	3 (3%)	0.31



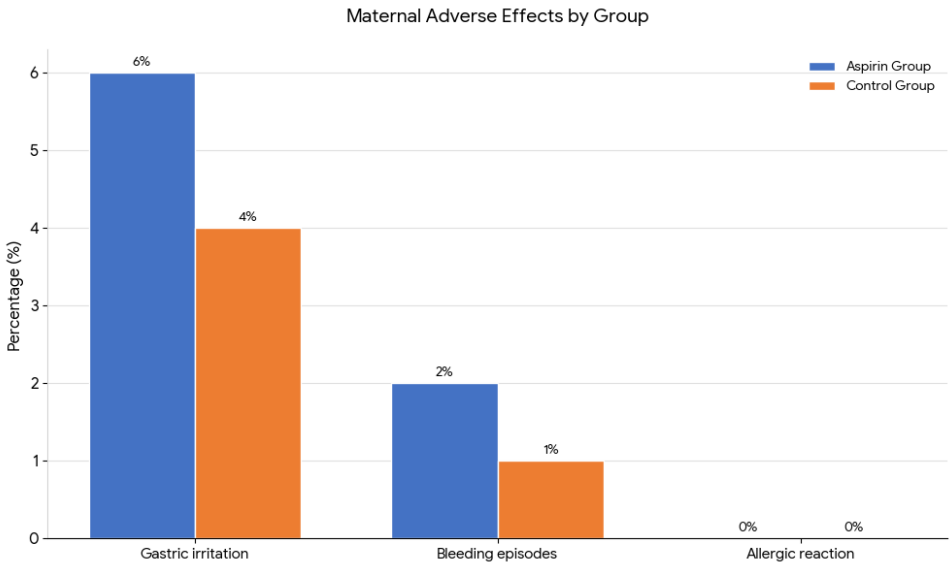
Graph 9: Neonatal Outcomes

10. Adverse Effects of Low-Dose Aspirin

Low-dose aspirin was well tolerated, with no significant increase in adverse maternal effects (Table 10)

Table 10: Adverse Effects of Low-Dose Aspirin

Adverse effect	Aspirin Group	Control Group	p-value
Gastric irritation	6 (6%)	4 (4%)	0.52
Bleeding episodes	2 (2%)	1 (1%)	0.56
Allergic reaction	0	0	—



Graph 10: Adverse Effects of Low-Dose Aspirin

DISCUSSION

The present prospective comparative study demonstrates that early initiation of low-dose aspirin (≤16 weeks of gestation) in high-risk pregnancies significantly reduces the incidence and severity of pregnancy-induced hypertension (PIH) and improves fetomaternal outcomes. The baseline demographic characteristics and distribution of high-risk factors were comparable between the aspirin and control groups, confirming that the observed differences in outcomes can be attributed to aspirin prophylaxis rather than confounding variables.

In our study, the incidence of PIH was significantly lower in the aspirin group (18%) compared to the

control group (34%), which is consistent with multiple systematic reviews and meta-analyses showing a protective effect of early aspirin initiation. Cui et al. (2018) reported a 33% reduction in pre-eclampsia when aspirin was started at or before 16 weeks, with a stronger effect on preterm disease [11]. Similarly, Xu et al. (2015) found that aspirin use before 16 weeks significantly reduced pre-eclampsia, preterm birth, and IUGR in high-risk women [12].

The severity of hypertensive disorders was also reduced in the aspirin group, with significantly fewer cases of severe pre-eclampsia, aligning with findings from Indian and international studies. Movva and Hota (2020) reported milder disease and reduced maternal morbidity in women receiving low-dose aspirin before 16 weeks [13]. The delayed onset of hypertension observed in our aspirin group further supports the hypothesis that aspirin improves early placentation and uteroplacental blood flow.

Our findings of reduced fetal growth restriction, low birth weight, preterm delivery, and NICU admissions are comparable to the ASPIRIN trial by Hoffman et al. (2020), which included Indian centers and demonstrated improved neonatal survival and reduced hypertensive complications with early aspirin initiation [14].

Importantly, low-dose aspirin was well tolerated in our study, with no significant increase in bleeding or postpartum hemorrhage, corroborating safety data from large meta-analyses (Komoróczy et al., 2025) [15].

In conclusion, our study reinforces existing evidence that early low-dose aspirin is an effective, safe, and cost-effective strategy for preventing PIH and improving fetomaternal outcomes in high-risk pregnancies, particularly relevant to the Indian healthcare setting.

CONCLUSION

Early initiation of low-dose aspirin at or before 16 weeks of gestation significantly reduced the incidence and severity of pregnancy-induced hypertension in high-risk pregnancies. Aspirin prophylaxis was associated with delayed onset of hypertension, reduced need for antihypertensive therapy, and improved maternal outcomes without increasing adverse effects. Favorable fetal outcomes, including lower rates of fetal growth restriction, preterm birth, and NICU admissions, further support its benefit. Early low-dose aspirin represents a safe, effective, and feasible preventive strategy in high-risk pregnancies, particularly in resource-limited settings.

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