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Original Research Article

EFFECT OF LOW DOSE ASPIRIN IN PREVENTION OF SPONTANEOUS PRETERM LABOUR

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ABSTRACT

Background: *Preterm birth remains a significant cause of neonatal morbidity and mortality worldwide. Preventive strategies in high-risk pregnancies are crucial to improving perinatal outcomes. Low-dose aspirin, with its antiplatelet and anti-inflammatory effects, has been proposed to reduce the risk of preterm delivery when added to standard care.* ***Objective:*** *To evaluate the outcome of low-dose aspirin versus placebo in addition to the standard treatment protocol in high-risk pregnant women for preterm birth.* ***Study Design:*** *Randomised controlled trial.* ***Setting:*** *Department of Obstetrics and Gynecology III at Services Hospital, Lahore, Pakistan.* ***Duration of Study:*** *From 22-June-2024 to 22-April-2025.* ***Methods:*** *A total of 382 pregnant women aged 18–45 years with a history of prior preterm delivery were enrolled and randomized into two groups. Group A received low-dose aspirin (75 mg/day from 14–36 weeks of gestation) plus standard care (including progesterone therapy and infection management), while Group B received a placebo plus standard care. The primary outcome was the incidence of spontaneous preterm birth (<37 weeks of gestation). Statistical analysis was performed using SPSS version 23, and $p < 0.05$ was considered significant.* ***Results:*** *The mean age of participants was 28.79 ± 7.28 years in Group A and 29.08 ± 7.33 years in Group B. The incidence of spontaneous preterm birth was significantly lower in the aspirin group (9.4%) compared to the placebo group (17.8%) ($p = 0.01$).* ***Conclusion:*** *Low-dose aspirin, when administered in addition to standard therapy, significantly reduces the incidence of spontaneous preterm birth in high-risk pregnant women. This suggests a beneficial role for aspirin prophylaxis in improving perinatal outcomes among women with a history of preterm delivery.*

Keywords: Low-Dose Aspirin, Spontaneous Preterm Labor, Preterm Birth, High-Risk Pregnancy

INTRODUCTION

A variety of biochemical as well as biophysical markers have been identified, suggested to identify patients at risk of spontaneous preterm delivery, useful to both those experiencing threatened preterm labor as well as asymptomatic individuals, to facilitate interventions that avoid preterm delivery (1-3). Recent studies show that ultrasound examination of the cervix is more effective compared to vaginal digital examination (4). In cases of patients with preterm labor, this method can aid in determining the risk of preterm delivery before 34 weeks. A shorter cervix is usually linked with an increased risk of preterm delivery, whereas a longer cervix relates to a lower risk (1-5). Sonography is an effective strategy for evaluating the risk of preterm delivery in individuals with preterm labor and those identified as high risk (6, 7).

Given similarities in mechanisms underlying spontaneous preterm labor as well as pre-eclampsia, it was proposed that low-dose aspirin might be used as a preventative therapy for spontaneous preterm labor. Several studies have carried out secondary analyses of information regarding the impact of low-dose aspirin on pre-eclampsia prevention to evaluate its effect on the prevention of preterm labor. While some studies have suggested potential benefits of low-dose aspirin in preventing preterm labor, others have failed to substantiate these findings (8-11). Furthermore, a study was conducted to evaluate the impact of low-dose aspirin on the occurrence of preterm labor; however, the clinical outcomes have yet to be disclosed (12). A study reported a reduction in the frequency of spontaneous preterm labor among mothers receiving regular low-dose aspirin. Specifically, 8.3% of high-risk mothers developed the adverse effect compared to 16.7% in the placebo group, in addition to the standard treatment protocol (13).

This study aims to evaluate whether the addition of low-dose aspirin to standard therapy is more effective than placebo in reducing the frequency of spontaneous preterm birth among high-risk pregnant women, potentially providing a simple, low-cost intervention to improve perinatal outcomes in this vulnerable population.

METHODOLOGY

This randomized controlled trial was conducted in the Department of Obstetrics and Gynecology-III at Services Hospital, Lahore, from 22 June 2024 to 22 April 2025, after obtaining ethical approval from the hospital. Three hundred and eighty-two women were enrolled; the sample was based on a one-sided hypothesis test for two population proportions. The anticipated proportions were derived from previous research with an assumed significance level (α) of 5% a test power (1-β) of 80% and expected frequencies of spontaneous preterm birth at 0.083% in the aspirin group and 0.167% in the placebo group.[13] Consecutive non-probability sampling was used. Women aged 18 to 45 years, with a history of preterm birth, were selected for this trial. Women with multiple gestations, premature rupture of membranes, cervical incompetence, chronic conditions such as hypertension or diabetes, bleeding disorders, peptic ulcer disease, or aspirin allergies were eliminated.

After obtaining consent from the patients, they were randomized into two groups using block randomization (191 women per group). Group A received 75 mg of aspirin daily from 14 weeks until 36 weeks of gestation alongside standard treatment (oral progesterone and management of infections), while Group B received a placebo in addition to standard care. Baseline demographic and obstetric history were recorded. Follow-up continued until delivery, with outcomes assessed based on the occurrence of spontaneous preterm labor, defined as delivery before 37 weeks following spontaneous contractions. SPSS 26 was used for analyzing the data. Variables examined included maternal age, BMI, parity, gestational age at presentation, and past obstetric complications such as gestational

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diabetes and recurrent infections. Descriptive statistics (mean and SD, along with frequencies and percentages) were used to evaluate the variables. The chi-square test compared outcomes between groups; p-values ≤ 0.05 were deemed notable—stratification was performed for demographic and obstetric history.

RESULTS

We evaluated two groups, Group A (low-dose aspirin) and Group B (placebo). In Group A, the mean age of patients was 28.79 ± 7.28 years, the mean gestational age was 24.54 ± 6.12 weeks, and the BMI was 24.98 ± 1.13 kg/m². Group B had similar baseline characteristics, with a mean age of 29.08 ± 7.33 years, a gestational age of 24.58 ± 6.43 weeks, and a BMI of 24.96 ± 1.12 kg/m².

The gender distribution of the fetuses was comparable, with 89 (46.6%) males in Group A and 99 (51.8%) males in Group B (Figure 1). History of gestational diabetes mellitus (GDM) was reported in 28 (14.7%) patients in Group A and 31 (16.2%) in Group B (Table 1).

The primary outcome, spontaneous preterm labor, occurred in 18 (9.4%) cases in Group A compared to 34 (17.8%) in Group B; we observed a statistically significant reduction with low-dose aspirin (p = 0.01) (Table 2). Stratification of the comparison of spontaneous preterm labor by various demographic and clinical presentations is shown in Table 3.

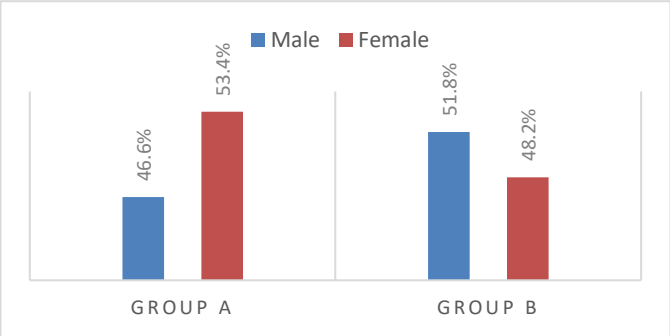

Figure 1: Gender distribution of the fetus

Table 1: Obstetric history of the patients

Obstetric history		Groups			
		Group A (Low-dose aspirin)		Group B (Placebo)	
		N	%	N	%
History of GDM	Yes	28	14.7%	31	16.2%
	No	163	85.3%	160	83.8%
History of preterm labor	Yes	69	36.1%	53	27.7%
	No	122	63.9%	138	72.3%
History of recurrent infection	Yes	13	6.8%	17	8.9%
	No	178	93.2%	174	91.1%
Parity	0 to 2	88	46.1%	86	45.0%
	> 2	103	53.9%	105	55.0%

Table 2: Comparison of spontaneous preterm labor between both groups

		Groups				P value
		Group A (Low-dose aspirin)		Group B (Placebo)		
		N	%	N	%	
Spontaneous preterm labor	Yes	18	9.4%	34	17.8%	0.01
	No	173	90.6%	157	82.2%	

Table 3: Stratification of comparison of spontaneous preterm labor between both groups with respect to demographic and obstetric history

				Groups				P value
				Group A (Low-dose aspirin)		Group B (Placebo)		
				N	%	N	%	
Gender of fetus	Male	Spontaneous preterm labor	Yes	9	10.1%	19	19.2%	0.08
			No	80	89.9%	80	80.8%	
	Female	Spontaneous preterm labor	Yes	9	8.8%	15	16.3%	0.11
			No	93	91.2%	77	83.7%	
History of GDM	Yes	Spontaneous preterm labor	Yes	3	10.7%	6	19.4%	0.35
			No	25	89.3%	25	80.6%	
	No	Spontaneous preterm labor	Yes	15	9.2%	28	17.5%	0.02
			No	148	90.8%	132	82.5%	
History of recurrent infection	Yes	Spontaneous preterm labor	Yes	5	38.5%	6	35.3%	0.85
			No	8	61.5%	11	64.7%	
	No	Spontaneous preterm labor	Yes	13	7.3%	28	16.1%	0.01
			No	165	92.7%	146	83.9%	
Parity	0 to 2	Spontaneous preterm labor	Yes	14	15.9%	14	16.3%	0.94
			No	74	84.1%	72	83.7%	
	> 2	Spontaneous preterm labor	Yes	4	3.9%	20	19.0%	0.001
			No	99	96.1%	85	81.0%	
Age distribution (Years)	18 to 30	Spontaneous preterm labor	Yes	16	14.0%	18	16.2%	0.64
			No	98	86.0%	93	83.8%	

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	31 to 45	Spontaneous preterm labor	Yes	2	2.6%	16	20.0%	0.001
			No	75	97.4%	64	80.0%	
Gestational age (Weeks)	14 to 25	Spontaneous preterm labor	Yes	6	5.9%	24	23.1%	0.001
			No	95	94.1%	80	76.9%	
	26 to 36	Spontaneous preterm labor	Yes	12	13.3%	10	11.5%	0.71
			No	78	86.7%	77	88.5%	
BMI (Kg/m2)	18 to 24.9	Spontaneous preterm labor	Yes	10	10.0%	14	13.7%	0.41
			No	90	90.0%	88	86.3%	
	> 24.9	Spontaneous preterm labor	Yes	8	8.8%	20	22.5%	0.01
			No	83	91.2%	69	77.5%	

DISCUSSION

Our results showed a statistically notable reduction in spontaneous preterm labor among women receiving low-dose aspirin compared to those in the placebo group, with rates of 9.4% versus 17.8% respectively (p = 0.01). Mirzamoradi et al. investigated low-dose aspirin in women with a history of preterm delivery. They found that while aspirin reduced the incidence of preterm birth, the reduction was not significant (p = 0.069). However, their subgroup analysis exhibited a notable decrease in preterm birth among women who experienced spontaneous labor (45% in the aspirin group vs. 80% in the placebo group, p = 0.022) (14). This resonates with our findings, which showed that aspirin had a pronounced effect on reducing spontaneous preterm labor. This can be attributed to aspirin's anti-inflammatory properties, which may mitigate the inflammatory pathways associated with spontaneous labor. Silver et al. conducted a trial and reported a notable reduction in preterm birth in women on a low aspirin dose compared with the placebo group (15).

Kupka et al. found that low-dose aspirin was linked with a reduced risk of preterm birth, particularly spontaneous preterm birth. This large-scale study supports our findings, reinforcing the idea that aspirin may be more effective in preventing spontaneous preterm birth than medically indicated preterm birth (8). The consistency across these studies suggests that aspirin's mechanism of action, likely through cyclooxygenase inhibition and reduced levels of inflammatory mediators, plays a key role in preventing spontaneous labor. In contrast to our findings, Landman et al found no potential decrease in preterm labor with aspirin (16).

One notable difference between our study and others is the baseline characteristics of the participants. Our cohort had a higher proportion of women with a history of preterm labor, which may have possibly influenced the observed effect size. This discrepancy could be attributed to differences in study design, sample size, or treatment adherence.

The dosage and timing of aspirin administration also appeared to influence the outcomes. Our study used a daily dose of 75 mg of aspirin from the 14th week of gestation until the 36th week, which is similar to Mirzamoradi et al., who used 80 mg daily (14). In contrast, Kupka et al. 2023) included varying doses (75–160 mg) yet still observed a protective effect (16). This implies that even lower doses may be effective in reducing the incidence of spontaneous preterm labor, though we suggest further research is needed to determine the optimal dosage. The timing of aspirin initiation is another critical factor. Silver et al. debated that preconception low-dose aspirin had a more pronounced effect when given before the 16th week of gestation than after (15). In our study, we initiated the dosage from the 14th week, confirming the claim of the study above.

Our findings infer that low-dose aspirin is a promising preventive measure for spontaneous preterm labor, particularly in high-risk women. Future research should focus on identifying biomarkers or clinical predictors to target aspirin therapy better. Additionally, larger randomized controlled trials with standardized protocols for dosage and timing are needed to confirm these findings and refine clinical guidelines.

CONCLUSION

We conclude that low-dose aspirin was notably effective than placebo, along with the standard treatment protocol, in high-risk pregnant women for preterm birth in terms of reducing the frequency of spontaneous preterm birth.

DECLARATIONS

Data Availability Statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department Concerned. (IRB)
Consent for publication
Approved
Funding
Not applicable

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

SIDRA MAQSOOD (PGR)
Data collection, Data analysis, Review of manuscript, Manuscript drafting and final approval of manuscript.
ROBINA FARRUKH (Professor)
Supervision, Study Design, Conception of Study, Final approval of manuscript.

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