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Low Dose Aspirin for Primary Prevention of Adverse Pregnancy Outcome

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Abstract

Background: Pregnancy is associated with various complications such as pre-eclampsia, SGA, preterm birth etc. Low dose aspirin is a possible medication to minimize these adverse outcomes. The aim of this study was to evaluate the use of low dose aspirin for primary prevention of adverse pregnancy outcome. **Material & Methods:** This cross-sectional study was conducted in department of Gynaecology, North Bengal Medical College Hospital, Mirjapur Bkash Hospital, Mirjapur, Tangail, Bangladesh, during the period from June 2021 to August 2022. Total 200 pregnant women were included in this study. **Results:** In this study, the mean (±SD) age of the study subjects were 25.12 ± 5.49 years and 25.00 ± 4.83 years in LDA group and control group, respectively. There was no statistically significant ($p>0.05$) difference in age between the groups. The rate of caesarean section was higher in control group (68%) compared to LDA group (59%) but there was no statistically significant ($p>0.05$) difference among the groups. In our study, 8% pregnant women in LDA group and 19% pregnant women in control group had gestational hypertension, pre-eclampsia was seen in 6% and 13% pregnant women in LDA group and control group, respectively, preterm birth was seen in 8% and 17% pregnant women in LDA group and control group, respectively, SGA was seen in 19% and 32% pregnant women in LDA group and control group, respectively, and fetal distress was seen in 2% pregnant women in both LDA group and control group. There were statistically significant ($p<0.05$) differences in complications except fetal distress. Mean (±SD) neonatal birth weight was 2.88±1.03 kg and 2.74±0.85 kg in LDA group and control group, respectively and there was no statistically significant ($p>0.05$) difference. **Conclusion:** We found that low dose aspirin could significantly reduce the risk of adverse outcomes, especially for pre-eclampsia, SGA and preterm birth.

Keywords:- Low Dose Aspirin, Primary prevention, and Adverse Pregnancy Outcome.

INTRODUCTION

The rising morbidity and mortality linked to preterm birth (PTB), preeclampsia (PE), and small for gestational age (SGA) during pregnancy continue to be serious problems on a global scale. Although the exact cause of these issues is yet unknown, elevated inflammation

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and/or hypoxia are frequently linked to their development.[1,2,3,4] Preterm delivery, defined as birth before 37 weeks of pregnancy, is the main contributor to newborn death, is linked to long-term impairment in survivors, and places a significant financial burden on healthcare and social services.[5] Low-dose aspirin is useful for lowering the risk of preeclampsia and its associated consequences, including preterm delivery, according to a meta-analysis of trial data.[6] Reanalysis of data from aspirin preeclampsia prevention studies also revealed minor but statistically significant decreases in spontaneous preterm delivery (preterm birth preceded by the spontaneous commencement of contractions or preterm pre-labor membrane rupture).[7,8] Pre-eclampsia is characterized by elevated blood pressure (hypertension) and proteinuria (protein in the urine).[9] Between 2% and 8% of pregnancies are complicated by it, which happens in the second half of pregnancy.[10,11,12,13] It contributes significantly to maternal, fetal, and neonatal morbidity and mortality, causing over 40,000 maternal deaths annually across the globe.[14] According to aspirin-dose-response studies, taking aspirin regularly lowered the incidence of preeclampsia and fetal growth restriction by 40-50%.[15,16,17] If aspirin treatment began before to 16 weeks of gestation, the impact seemed to be more pronounced.[18] But regardless of whether the prophylactic started before or after 16 weeks, a single person pooled study revealed that the effectiveness of low-dose aspirin was substantially less (a decrease of about 10% for preeclampsia).[19] For the greatest prophylactic impact, low-dose aspirin should be started at 12 weeks' gestation and continued until birth, according to obstetric clinical recommendations.[20,21] Pre-eclampsia can also have an adverse effect on the liver, kidneys, and brain of the mother, as well as cause irregularities in the clotting system.[22] The most frequent ones are issues with premature birth and poor development brought on by insufficient blood flow through the placenta.[23] Aspirin is a desirable target for avoiding gestational hypertension diseases due to its well-described anti-inflammatory and anti-coagulation capabilities, although the precise mechanism is still unknown.16 Recent research has improved our knowledge of aspirin's effects on the prevention of PE, PTB, and SGA.[19,24,25] In order to avoid negative outcomes and reduce the risk of postpartum hemorrhage, the American College of Obstetricians and Gynecologists (ACOG) advises daily low-dose aspirin (81 mg/day) throughout pregnancy.[26] However, a different meta-analysis found that a dosage of aspirin between 100 and 150 mg was preferable, particularly if started before 16 weeks.18 There is still disagreement on the ideal dosage. There is need to study more to see the proper effect of low dose aspirin for primary prevention of adverse pregnancy outcome. Thus, this current study was conducted to evaluate the use of low dose aspirin for primary prevention of adverse pregnancy outcome.

Objectives

To evaluate the use of low dose aspirin for primary prevention of adverse pregnancy outcome.

MATERIAL AND METHODS

This cross-sectional study was conducted in department of Gynaecology, North Bengal Medical College Hospital, Mirjapur Bkash Hospital, Mirjapur, Tangail, Bangladesh,

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during the period from June 2021 to August 2022. Total 200 pregnant women were included in this study. The study people were divided into two groups; 100 pregnant women in low dose aspirin (LDA) group and 100 pregnant women in control group. Aspirin 75 mg was prescribed to take per night from recruitment until 35 weeks of gestational age. Consent of the patients and guardians were taken before collecting data. After collection of data, all data were checked and cleaned. After cleaning, the data were entered into computer and statistical analysis of the results being obtained by using windows-based computer software devised with Statistical Packages for Social Sciences version (SPSS) 22. Numerical variables were expressed as mean and standard deviation, whereas categorical variables were count with percentage. Quantitative data among groups were analyzed by ANOVA test followed by exploration of significant difference between all possible paired group means by Bonferroni test. P value of less than 0.05 was considered statistically significant.

Inclusion Criteria

- Child bearing age groups

Exclusion Criteria

- Patients with chronic disease
- Patients transferred to another hospital

RESULTS

[Table 1] demonstrates the comparisons of baseline characteristics between LDA group and control groups. In this study, the mean (±SD) age of the study subjects were 25.12 ± 5.49 years and 25.00 ± 4.83 years in LDA group and control group, respectively. There was no statistically significant ($p>0.05$) difference in age between the groups. Mean (±SD) BMI were 27.24 ± 4.35 kg/m2 and 27.55 ± 4.88 kg/m2 in LDA group and control group, respectively. Majority pregnant women were in multigravida group in both LDA group (53%) and control group (58%) and there was no statistically significant ($p>0.05$) difference among the groups. Mean gestational age in LDA group was 38.10 weeks (SD±2.28 weeks) and in control group 37 weeks (SD±1.22 weeks) with statistically significant ($p<0.05$) difference. [Figure 1] demonstrates the comparisons of pregnancy related comorbidities between LDA group and control group. Majority pregnant women had gestational diabetes militias (GDM) group in both LDA group (17%) and control group (23%), hypothyroidism was seen in 15% and 16% pregnant women in LDA group and control group. [Table 2] shows the comparisons of maternal complications and outcomes between LDA group and control group. The rate of caesarean section was higher in control group (68%) compared to LDA group (59%) but there was no statistically significant ($p>0.05$) difference among the groups. In our study, 8% pregnant women in LDA group and 19% pregnant women in control group had gestational hypertension, pre-eclampsia was seen in 6% and 13% pregnant women in LDA group and control group, respectively, preterm birth was seen in 8% and 17% pregnant women in LDA group and control group, respectively, and SGA was seen in 19% and 32% pregnant women in LDA group and control group, respectively. There were statistically significant ($p<0.05$) differences in complications. [Table 3] shows the comparison of neonatal outcome between LDA group and control groups. Mean (±SD) neonatal birth weight was 2.88±1.03 kg

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and 2.74±0.85 kg in LDA group and control group, respectively and there was no statistically significant (p>0.05) difference. Mean (±SD) Apgar score at the first minute were 7.30 ± 0.69 and 7.07 ± 0.89 in LDA group and control group, respectively. Mean (±SD) Apgar score at the fifth minute were 8.47 ± 0.62 and 8.03 ± 0.87 in LDA group and control group, respectively. There were statistically significant (p<0.05) differences in both Apgar scores. Majority of the newborn were female in both LDA group (54%) and control group (55%) and there was no statistically significant (p>0.05) difference among the groups.

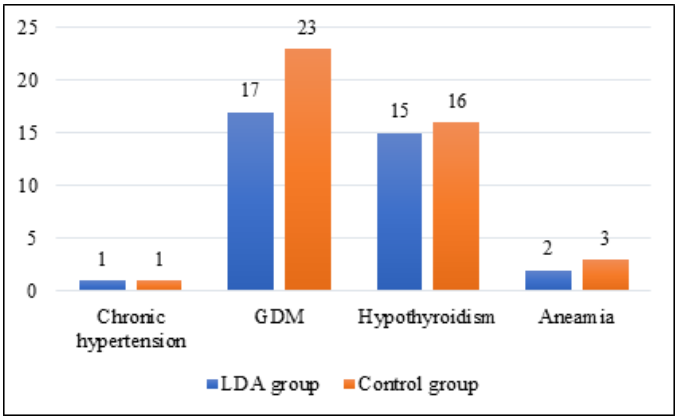

Figure 1: Comparisons of pregnancy related comorbidities between LDA group and control groups. (n=200)

Table 1: Comparisons of baseline characteristics between LDA group and control groups. (n=200)

Parameters		**LDA group (n=100)**	**Control group (n=100)**	**p value**
Maternal age (years)	Mean ± SD	25.12 ± 5.49	25.00 ± 4.83	0.8698^{ns}
BMI (kg/m2)	Mean ± SD	27.24 ± 4.35	27.55 ± 4.88	0.6359
Para	Primi	47 (47%)	42 (42%)	0.4779^{ns}
	Multi	53 (53%)	58 (58%)	
Gestational age (weeks)	Mean ± SD	38.10 ± 2.28	37.00 ± 1.22	< 0.0001^{s}

P value reached from unpaired t-test
s= Significant (p<0.05), ns = Not Significant (p>0.05)

Table 2: Comparisons of maternal complications and outcomes between LDA group and control groups. (n=200).

Parameters		**LDA group (n=100)**		**Control group (n=100)**		**p value**
		n	**%**	**n**	**%**	
Mode of delivery	Caesarean section	59	59	68	68	0.1873^{ns}
	Normal delivery	41	41	32	32	
Complications	Gestational hypertension	8	8	19	19	0.0232^{s}
	Pre-eclampsia	6	6	13	13	0.0384^{s}
	Preterm birth	8	8	17	17	0.0300^{s}
	SGA	19	19	32	32	0.0354^{s}

P value reached from unpaired t-test
s= Significant (p<0.05), ns = Not Significant (p>0.05)

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Table 3: Comparison of neonatal outcome between LDA group and control groups. (n=200)

Parameters		LDA group (n=100)	Control group (n=100)	p value
Neonatal weight (kg)	Mean ± SD	2.88±1.03	2.74±0.85	0.2958^{ns}
Apgar score				
At the first minute	Mean ± SD	7.30 ± 0.69	7.07 ± 0.89	0.0424^{s}
At the fifth minutes		8.47 ± 0.62	8.03 ± 0.87	0.0001^{s}
Sex of newborn (%)	Male	46 (46%)	45 (45%)	0.8874^{ns}
	Female	54 (54%)	55 (55%)	

P value reached from unpaired t-test
s= Significant (p<0.05), ns = Not Significant (p>0.05)

DISCUSSION

In this study, the mean (±SD) age of the study subjects were 25.12 ± 5.49 years and 25.00 ± 4.83 years in LDA group and control group, respectively. There was no statistically significant (p>0.05) difference in age between the groups. Mean gestational age in LDA group was 38.10 weeks (SD±2.28 weeks) and in control group 37 weeks (SD±1.22 weeks) with statistically significant (p<0.05) difference. In the study of Ye Y et al,[27] the mean gestational age in LDA group was 259 days or 37 weeks and in control group 254 days or 36.29 weeks. Here, gestational age at delivery has increased in LDA group which is similar to our study. Majority pregnant women had gestational diabetes militias (GDM) group in both LDA group (17%) and control group (23%), hypothyroidism was seen in 15% and 16% pregnant women in LDA group and control group. Schisterman EF et al,[28] found 2% GDM in both groups. In another study of Ye Y et al,[27] there was no statistically significant differences in GDM, hypothyroidism and anemia. The rate of caesarean section was higher in control group (68%) compared to LDA group (59%) but there was no statistically significant (p>0.05) difference among the groups. In the study of Wei Gu et al,[29] lower rate of caesarean section was performed in LDA group compared to placebo group. Occurrence of PE in our study was significantly (p<0.05) lower in LDA-treated mothers which is consistent with other studies. Large meta-analyses and thorough reviews have repeatedly demonstrated that LDA is successful in lowering the incidence of PE.[15,30,31,32,33] Recent research from the Aspirin for Evidence-based Preeclampsia Prevention (ASPRE) trial has shown that aspirin at a daily dose of 150 mg, started before 16 weeks of gestation, and administered at night to a high-risk population identified by a combined first-trimester screening test, lowers the incidence of preterm pre-eclampsia by 62% in comparison to placebo.[34] Euser et al,[35] also found similar findings. We found that, preterm birth (PTB) was significantly (p<0.05) lower in LDA-treated mothers. PTB's multifactorial onset might involve endocrine and immunological problems, uterine overdistention, or inflammation.[36,37,38] It has also been demonstrated that vascular diseases and placental ischemia contribute to the etiology of PTB.[39,40] Aspirin has the potential to reduce the activity of various inflammatory factors and

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enhance placental blood flow, which might hypothetically reduce the prevalence of PTB. Aspirin shown significant advantages in singletons avoiding PTB in clinical settings.[8,24,41] LDA was only linked to a drop in PTB 34w in singletons in Andrikopoulou's research.[24] The SGA rate was also significantly ($p<0.05$) lower in LDA-treated mothers in our current study. The mean (±SD) neonatal birth weight was 2.88±1.03 kg and 2.74±0.85 kg in LDA group and control group, respectively but there was no statistically significant ($p>0.05$) difference. There has been discussion on whether LDA might lower SGA.[15,42] Bergeron et al.[43] concentrated on several gestations and came to the conclusion that LDA did not reduce the incidence of SGA. However, early begun LDA might lower the risks of SGA in a different meta-analysis for singletons.[15] Therefore, precaution is required to avoid adverse pregnancy outcomes for both mother and child. Large-scale research is needed on the use of low dosage aspirin to avoid adverse pregnancy outcomes.

Limitations of The Study

In our study, there was small sample size and absence of control for comparison. Study population was selected from only Tangail, so may not represent wider population. The study was conducted at a short period of time.

CONCLUSIONS

We found that low dose aspirin could significantly reduce the risk of adverse outcomes, especially for pre-eclampsia, SGA and preterm birth. Further study with large population and different LDA dose is need to be done to have better understanding.

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