ASSESSING THE EFFECTIVENESS OF LOW-DOSE ASPIRIN AS A PROPHYLACTIC INTERVENTION FOR THE PREVENTION OF HYPERTENSIVE DISORDERS IN PREGNANCY: A COMPREHENSIVE ANALYSIS

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ABSTRACT

Objective: To assess if using modest doses of aspirin can prevent hypertensive problems in pregnant women.

Methods: An investigation was carried out in the Department of Obstetrics and Gynecology of the Qazi Hussain Ahmed Medical Complex, Nowshera, Pakistan, from October 1, 2019, to March 30, 2020. 177 pregnant women who were deemed to be at high risk for hypertension issues participated in the study. Every patient was given 75 mg of aspirin every day until they reached 37 weeks of pregnancy. Determining the intervention's operational efficacy was a key focus of the study.

Results: Participants in this research ranged in age from 18 to 35 years old, with a mean age of 29.559±2.54 years. 13.355±1.39 weeks was the average gestational age; 73.113±13.30 kg was the mean weight; 73.113±13.30 meters were the mean height; and 29.609±4.89 kg/m2 was the mean BMI. In 74% of the patients, the intervention was found to be beneficial.

Conclusion: The findings of this study validate the use of low dosage aspirin therapy as a preventive measure against early preeclampsia and preeclampsia.

Keywords: Pregnancy, high risk for hypertensive disorder, Low-dose aspirin, preeclampsia, gestational age

INTRODUCTION

Currently, aspirin is the most commonly recommended medication for preventing cardiovascular problems.[1] One Aspirin is commonly utilised in small amounts to prevent vascular problems associated with pregnancy, such as preeclampsia and intrauterine growth restriction. It is also used to prevent maternal disorders such antiphospholipid syndrome.

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The indications for administering aspirin during pregnancy are currently a topic of significant dispute. The effectiveness of this treatment has not been shown in many of these cases, yet, it is being recommended to a growing percentage of pregnant women.[2]

Aspirin, known as acetylsalicylic acid, undergoes a transformation into salicylic acid. This acid molecule undergoes acetylation of a serine residue located at the active region of COX enzyme, hence inhibiting the binding of arachidonic acid. The inhibition of the catalytic site of COX is contingent on the dosage, and it is characterised by stability, covalence, and irreversibility. Aspirin mostly inhibits the constitutive COX-1 enzyme, with less inhibition occurring for the inducible COX-2 enzyme. The ability of the cell to produce new COX determines how long aspirin acts.[3]

To prevent preeclampsia (PE), women with a history of chronic hypertension, type 1 or type 2 diabetes, autoimmune or renal disease, or multiple pregnancies should take low-dose aspirin, according to the American College of Obstetricians and Gynecologists (ACOG) and

the US Preventive Services Task Force (USPSTF).[4] Four meta-analyses of randomised controlled trials (RCTs) comparing aspirin to placebo or no treatment have demonstrated that aspirin, when initiated at or before 16 weeks of gestation, can effectively reduce the occurrence of PE. This effect is particularly pronounced in cases of severe PE resulting in delivery before 34 weeks of gestation. However, starting aspirin beyond 16 weeks of pregnancy had no discernible effect on the incidence of severe preeclampsia.[5] Pregnant women on low-dose aspirin had an 8% chance of developing preeclampsia, according to research by Ebrashy A. et al.[6] Low-dose aspirin showed an effectiveness rate of 33% in avoiding preeclampsia in pregnant women, according to another research by Cui Y. et al.[5]

However, the worldwide use of low-dose aspirin remains inconsistent, possibly due to the dispute surrounding its effectiveness. Several studies have indicated that administering low-dose aspirin does not have a substantial impact on the likelihood of developing preeclampsia.[7] Given the ongoing dispute on the outcomes in various populations, I intend to assess the effectiveness of administering a small dosage of aspirin in preventing hypertensive disease in expectant mothers. The findings of my research not only offer local empirical support but also, if the results encourage the use of low-dose aspirin, it can be implemented as a standard practice for patients with a high susceptibility to preeclampsia.

METHODOLOGY

From October 1st, 2019, to March 30th, 2020, descriptive research was conducted at the Department of Obstetrics and Gynecology at the Qazi Hussain Ahmed Medical Complex, Nowshera, using a 95% confidence interval, a 4% margin of error, and an expected effectiveness of 8%, the sample size was calculated using the WHO calculator. All women between the ages of 18 and 35 who were pregnant alone, had a gestational age of 11 to 15 weeks, and were at high risk of developing hypertensive disorders were included in the study. To choose participants, non-probability sequential sampling was used. The research excluded patients having a history of gastrointestinal ulcers, allergy to salicylates, or diabetes as documented in their medical records.

Following clearance from the ethics committee and research department of HMC, Peshawar, 177 patients who fit the inclusion criteria from the Department of Obstetrics and Gynecology (DOG) were recruited in the study. The following baseline demographic data was gathered: age, parity, gestational age, weight on a scale, height on a height scale, and BMI. Each patient gave their informed permission after being fully informed of the hazards involved in taking part in the trial, with confidentiality guaranteed.

Up to the time they reached 37 weeks gestation, all patients were provided a daily dosage of 75 mg of aspirin. Using a specifically created proforma, the researcher evaluated and documented the efficacy in accordance with the operational definition. PSS version 22, a statistical analysis application, was used to analyze the data. For quantitative factors including age, weight, gestational age, height, and BMI, the mean ±SD was given. Calculations were made for frequency and percentage for qualitative factors such as effectiveness and parity. Using stratification, effect modifiers including age, parity, gestational age, and BMI were managed. Using a post-stratification chi-square test, statistical significance was determined at $p \leq 0.05$.

RESULTS

The study included participants aged 18 to 35 years. The average age was 29.559±2.54 years. The average gestational age was 13.355±1.39 weeks. The average weight was 73.113±13.30 kg. The average height was 1.572±0.10 meter. The average BMI was 29.609±4.89 kg/m2, as indicated in Table-I.

74% of patients demonstrated efficacy, as evidenced
in Table-II.

The categorization of effectiveness based on age, gestational age, parity, and BMI is displayed in Tables III, IV, V, and VI, correspondingly.

Table- I: Mean ± SD of patients according to age, gestational age, weight, height and BMI (n=177)

Demographics	Mean±SD
Age(years)	29.559±2.54
Gestational Age (weeks)	13.355±1.39
Weight (Kg)	73.113±13.30
Height (meters)	1.572±0.10
BMI (Kg/m^2)	29.609±4.89

Table- II: Frequency and %age of patients according to efficacy (n=177)

Efficacy	Frequency	%Age
Yes	131	74%
No	46	26%
Total	177	100%

Table-III: Categorization of effectiveness based on age.

Age (years)	Efficacy		p-value
	Yes	No	
18-30	79(73.8%)	28(26.2%)	0.946
>30	52(74.3%)	18(25.7%)	
Total	131(74%)	46(26%)	

Table-V: Classification of effectiveness based on gestational age.

Gestational Age (weeks)	Efficacy		p-value
	Yes	No	
11-13	62(75.6%)	20(24.4%)	0.652
14-15	69(72.6%)	26(27.4%)	
Total	131(74%)	46(26%)	

Table VI presents the categorization of effectiveness based on parity.

Parity	Efficacy		p-value
	Yes	No	
0-2	94(77%)	28(23%)	0.170
>2	37(67.3%)	18(32.7%)	
Total	131(74%)	46(26%)	

Table-VII presents the categorization of effectiveness based on BMI.

BMI (Kg/m^2)	Efficacy		p-value
	Yes	No	
≤30	100(100%)	0(0%)	0.000
>30	31(40.3%)	46(59.7%)	
Total	131(74%)	46(26%)	

DISCUSSION

Preeclampsia can be avoided by consuming a little dosage of aspirin, according to several research.[8] In this study, pregnant Pakistani women who are more likely to develop preeclampsia were examined to see if aspirin may prevent the illness. The findings of this study have substantiated the prophylactic impact of aspirin on expectant mothers who are at a heightened risk of developing preeclampsia. The two types of preeclampsia; regular and early were successfully avoided by administering a small dose of aspirin daily beginning in the eleventh to fifteenth week of pregnancy and continuing until birth. Following a review of the effects of various dosages, we recommend 75 mg for Pakistani pregnant women who are more likely to develop preeclampsia. Our study found that if a low dose of aspirin was administered between weeks 11 and 15, the risk of complications like restriction of fetal growth, postpartum hemorrhage, and premature delivery was significantly reduced. This, in turn, reduced the chance of requiring a cesarean section. There is no proof that the incidence of placental abruption and miscarriage differs from one another. It is crucial to organize high-risk variables into several categories to enhance the preventative effect of low-dose aspirin. As of right now, neither worldwide nor in Pakistan are there any pertinent guidelines accessible. This research proposes the creation of a preventative approach specific to preeclampsia risk groups to minimize needless drug usage during pregnancy. According to our research, aspirin was more beneficial for women whose uterine arterial resistance S/D was greater during the early stages of pregnancy. Our goal is to develop a regular screening procedure based on these results to evaluate the flow of blood through the uterine arteries during antenatal care. This will assist in identifying fetuses who may benefit from taking aspirin at a low dose. The Doppler-uterine artery test is a practical, affordable, and easy procedure. It may be advised that women with high-risk diseases like as preeclampsia and excessive uterine vascular resistance take aspirin. This method's viability is still being assessed, and more information is required before it can be put into practice.

Using aspirin to prevent placental vascular disease has advanced significantly since the publication of Beaufils et al. in 1985,[9] which first showed aspirin's effect on obstetrics. Multiple countries have issued guidelines endorsing the utilisation of low-dose aspirin in pregnant women at high risk of developing preeclampsia as a preventive measure. On the best aspirin dosage for preventing preeclampsia, there is still disagreement. Numerous studies have employed dosages ranging from 60 mg to 150 mg daily. To avoid high-risk preeclampsia, the World Health Organization (WHO) suggested taking 75 mg of aspirin daily in 2011.[10] The ACOG recommended in 2013 that women begin taking aspirin at the end of their first trimester at a dosage of 60–80 mg per day.[11] The US Preventive Services Task Force (USPSTF) found in a comprehensive review done in 2014 that aspirin's efficacy was unaffected by dose, maybe because various dosage categories had varied sample sizes.[12] As a preventative measure, commencing in the 12th week of pregnancy, the ACOG and the USPSTF recommendations prescribe 81 mg of medicine daily for high-risk women. [13,14] There is a dose-dependent effect of aspirin, according to a recent meta-analysis.[15] Research indicates that a larger dosage of aspirin is favorably connected with its efficiency.[16, 17] Large samples from several areas and more evidence-based prospective study will determine whether a higher dose is necessary in Pakistan. The findings of this research validate the protective value of aspirin in expectant mothers who are susceptible to preeclampsia. Sibai et al. discovered that aspirin is ineffective in modifying the course of preeclampsia once it has already begun, mostly because of placental characteristics such as shallow implantation.[18] To lessen the likelihood of pregnancy-induced hypertension, aspirin should be given as early in the pregnancy as possible, before the placenta has fully formed. The ACOG guidelines for hypertensive diseases in pregnancy state that in order to prevent preeclampsia, high-risk patients should begin taking aspirin as soon as their early pregnancy ends.[19] Several trials have stopped aspirin at different times, generally before to delivery.[20] According to Ayala et al., taking an aspirin eight hours after waking up and before bed proved to be more beneficial than taking it right away.[21] The circadian rhythm has a big impact on how effective medications are. Drugs given throughout the day have little effect on blood pressure management or the prevention of preeclampsia; nevertheless, when taken right before bed, they have noticeable effects. Pregnant women are thus advised to take low-dose aspirin prior to going to bed. Physicians need to be on the lookout for any dangers associated with aspirin usage for expectant women and fetuses. Aspirin frequently causes bleeding, gastrointestinal ulcers, allergic

responses, kidney and liver damage, neurotoxicity, and Rayleigh's syndrome as adverse effects. Because aspirin tends to cause bleeding during pregnancy and affects blood coagulation function, monitoring is necessary. It is widely accepted that doses between 60 and 150 mg are safe.[22] But it's important to remember that if the dosage is more than 150 mg, there is a much higher chance of bleeding.[23] Low-dose aspirin usage does not increase the risk of postpartum hemorrhage, placental abruption, or cerebral hemorrhage, according to many meta-analyses. Moreover, it doesn't raise the chance of perinatal death.[8, 24] Additionally, aspirin does not increase the risk of postpartum hemorrhage or placental abruption, according to clinical investigations.[12,25,26] Regardless of when the medication was started during gestation, the most recent meta-analysis showed that taking aspirin at a dose of less than 100 mg per day had no effect on the risk of antepartum hemorrhage or placental abruption.[27] Low-dose aspirin can promote the reshaping of spiral arteries and eventually prevent placental defects by increasing the flow of blood in the spiral arteries and facilitating trophoblast migration. Research in this field suggests that aspirin can lower the risk of placental problems, such as limited fetal development and spontaneous premature delivery.[28, 29]

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