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Original Article

Role of Antiplatelet Therapy For Prevention of Preeclampsia in High Risk Patients

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Abstract

Objective: To assess the efficacy of antiplatelet therapy to prevent pre eclampsia in high risk patients.

Methods: This descriptive case series study was carried out at Sir Ganga Ram Hospital, Lahore for duration of 6 months (from 28-11-2018 to 28-05-2019). Total 200 women were enrolled in the study fulfilling the inclusion criteria.Their demographic details were obtained after informed consent.All participants were given 120 mg/day of antiplatelet (Asprin), (NICE Guideline 107).They were followed-up in OPD till 36th week of gestation. If female developed BP≥140/90mmHg and proteinuria> 300mg on urine dipstick method, then preeclampsia was labeled. All this information was recorded on predesigned Performa. Complications of antiplatelet therapy like antepartum hemorrhage, acid peptic disease and low platelets were also recorded.

Results: The mean age of all females was 29.87 ± 5.82 years. There were 12(6%) females who had preeclampsia in previous pregnancy, 45(22.5%) were obese cases,16(8%) females had chronic hypertension, 138(69%) females had gestational hypertension and 37(18.5%) cases had gestational diabetes. The complications observed were preeclampsia in 25 (12.5%) cases, hemorrhage in 94(47%), acid peptic disease in 64(32%) and low platelet in 17(8.5%) cases.

Conclusion: It is concluded that the frequency of preeclampsia was very low among high risk females after having 120mg of Aspirin (antiplatelet therapy) in first trimester but the side effects of antiplatelet therapy do increase with the higher dose.

Keywords: Pregnancy, complications, preeclampsia, antiplatelet therapy

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Introduction

One of the major public health concern is Maternal Mortality and in less developed countries it accounts for >99 % of maternal deaths. Hemorrhage, sepsis, hypertension and its complications are common causes of direct maternal deaths.[1] Maternal Mortality Rate is 276 per 100,000 live births in Pakistan.[2] Deaths due to pre-eclampsia/eclampsia represent one-third of maternal deaths reported at the settings of tertiary care hospitals in Pakistan.[1] Around 2–10% of pregnant women are affected by preeclampsia and makes it a major cause of maternal and perinatal morbidity and mortality. For prevention of preeclampsia, various interventions like frequent antenatal visits, change in lifestyle, nutritional supplementation, and drugs have been studied.[3]

In the prevention of preeclampsia and its complications, the effect of antiplatelet agents has been established, regardless of whether the treatment is started before or after 12 weeks of gestation. Antiplatelet therapy prophylaxis should be considered in women who are at an increased risk of preeclampsia. The frequency of preeclampsia was reduced to 10.7% with antiplatelet therapy in high risk females in one study.[4] Another study showed that frequency of preeclampsia was 8.85% with antiplatelet therapy in high risk females.[5]

Preeclampsia developed in 3.7% cases with antiplatelet therapy according to one metaanaysis.[6] A systematic review showed that 16.1% females developed preeclampsia without antiplatelet therapy.[7]

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This study has been conducted to assess the frequency of preeclampsia with higher dose of antiplatelet therapy given before 12 weeks of gestation in high risk females. Literature has ambiguous results regarding efficacy of 120mg antiplatelet therapy. Also there is no proposed local study in this regard. So, this study was conducted to findout the efficacy and side effects of 120mg antiplatelet therapy in high risk females to prevent development of preeclampsia. The results will help to update local guidelines and can also help to change our current practice of pre-eclampsia prophylaxis with 75mg Antiplatelet therapy.

Methods

Study Design: Descriptive case series

Settings: Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital Lahore

Duration of Study: Six months, from November 28, 2018 till May 28, 2019.

Sample Size: Sample size of 200 cases was calculated with 95% confidence level, 4% margin of error and taking expected percentage of preeclampsia i.e 8.85% with antiplatelet therapy in high risk females.[5]

Sampling Technique: Non probability, consecutive sampling.

Sample Selection Criteria

Inclusion criteria: Females of age 20-40 years, parity <5 presenting in gestational age <12 weeks (according to LMP) for antenatal check-up for high risk pregnancy.

Exclusion criteria:

- Females with systemic problems i.e. deranged LFTs (ALT>40IU, AST>40IU, bilirubin> 5IU/L),
- Females deranged RFTs (creatinine>1.2mg/dl).
- Females with cardiac problem (abnormal ECG and medical record)
- Females with existing placenta previa
- Females with fibroid uterus in pregnancy (on ultrasound)

Data Collection Procedure

Total 200 females, fulfilling the selection criteria were recruited in this study from OPD of Department of Obstetrics & Gynecology, Sir Ganga Ram Hospital, Lahore. Informed consent was taken and demographic details(name,age, gestational age, parity and BMI) were recorded. All females were given 120mg/day of antiplatelet therapy (aspirin). All participants were followed-up monthly till 30 weeks and then fortnightly till 36 weeks of gestation for development of high BP, proteinuria or side effects of Aspirin. If female developed BP 140/90mmHg and proteinuria>+1 on dipstick method, then preeclampsia was labeled. All this information was recorded on pre-designed Performa. The females who developed preeclampsia were managed as per hospital protocol. Complications of antiplatelet therapy such as antepartum hemorrhage, acid peptic disease and low platelets were also recorded. Any patient developing any side effects was managed efficiently as per standard protocol.

Data Analysis

Data was entered and analyzed by SPSS version 21. Mean and SD was calculated for age, BMI and gestational age. Frequency and percentage was calculated for pre-eclampsia. Parity was presented as frequency. Data was stratified for age, gestational age, parity type of underlying condition and BMI. Post-stratification, chi-square test was used with P-value 0.05 taken as significant.

Results

The mean age of all participants was 29.87 ± 5.82 years with minimum and maximum age as 20 and 40 years respectively. The mean body mass index was 28.31 ± 2.55 with minimum and maximum BMI as 24 and 33.9kg/m^2 respectively. The mean gestational age was 33.54 ± 3.52 weeks with minimum and maximum gestational age as 28 and 39 weeks respectively. There were 81(40.5%) females who had parity <3 and 119(59.5%) females had parity as 3-4. There were 12(6%) females who had pre-eclampsia in previous pregnancy, there were 45(22.5%) obese cases, there were 16(8%) females who were chronic hypertensive, and 138(69%) females who had gestational hypertension and 37(18.5%) cases who had gestational diabetes. There were 25(12.5%) cases who developed preeclampsia, 94(47%) cases who had antepartum hemorrhage, 64(32%) cases had acid peptic disease and 17(8.5%) cases had low platelets.

The data was stratified for the age of the patient. In age group of 20-30 years, 11.3% of patients developed pre-eclampsia. In age group of 31-40 years 13.8% patients developed preeclampsia. The data was stratified

with respect to parity. In patients with parity<3, 17.3% patients developed preeclampsia and with parity 3-4, 9.2% patients developed preeclampsia. The data was stratified with respect to gestational age. In patients with gestational age 28-34 weeks, 10.8% patients developed preeclampsia, and with gestational age 34.1-39 weeks 14.3% patients developed preeclampsia. Data was stratified with respect to preeclampsia in previous pregnancy 33.3% patients developed preeclampsia and in patients with no history of preeclamsia the percentage was 11.2%. Data was stratified with obesity. In obese patients, the percentage of developing preeclampsia was 15.6% and in non-obese it was 11.6%. Data stratification with respect to chronic hypertension showed the percentage of development of preeclampsia with positive history of chronic hypertension as 0% and with no history as 13.6%.

Discussion

Development of hypertension and proteinuria after 20 weeks of gestation defines pre-eclampsia and is associated with increased risk of long term cardiovascular mortality for mother and infant[12]. The World Health Organization recommends administration of low dose aspirin (75 mg/day) should be started during early pregnancy to prevent preeclampsia in high risk females should[13]. Complications of preeclampsia, for example, perinatal death, preterm birth, and having a small for-gestational-age baby, are all reduced with the administration of anti-platelet agents. Although the benefits associated with antiplatelet agents are modest, they have public health importance, particularly because their safety is reassured, and aspirin is both easily available and cost effective 48. International guidelines recommend that women who are at an increased risk of preeclampsia should be offered aspirin. However, recommendation regarding timings to start the treatment vary ranging from before or at 12 weeks gestation to before 16 or 20 weeks. Whethe to commence treatment earlier in pregnancy has greater benefits, also remains controversial.[14]

Table 1: *Descriptive Statistics of Age(Years), BMI, Gestational Age in Weeks,*

		Age (years)	BMI	Gestational age(weeks)
Age (years)	n	200	200	200
	Mean	29.87	28.99	33.54
	SD	5.82	2.71	3.52
	Range	20.00	10.00	11
	Minimum	20.00	24.00	28
	Maximum	40.00	34.00	39

Table 2: *Frequency of Preeclampsia and Complications with Antiplatelet Therapy*

	Yes	No	Total
Preeclampsia	25	175	200
Antepartum haemorrhage	94	106	200
Acid peptic disease	64	136	200
Low platelets	17	183	200

Recently a meta-analysis study was conducted and demonstrated that there was significant reduction in overall risk ratio (RR) of preeclampsia regardless of the time of delivery, when compared with placebo or no treatment. It was concluded that when low dose aspirin was commenced at ≤16 weeks of gestation in women at increased risk of preeclampsia was associated with a reduction in overall risk of preterm preeclampsia, and of adverse maternal and neonatal outcomes[15]. Another meta-analysis concluded that there was no significant difference in the effects of antiplatelet therapy for women randomized before 16 weeks gestation compared with those randomized at or after 16 weeks. Antiplatelet therapy should be offered to women at increased risk of preeclampsia, regardless of whether they are first seen before or after 16 weeks gestation.[9]

Another study results showed the effect of aspirin dosage on the prevention of preeclampsia, severe preeclampsia, and fetal growth restriction. They reported that aspirin initiated at >16 weeks was not associated with reduce risk or a dose-response effect for severe preeclampsia and fetal growth restriction. There is no or modest effect on the risk of preeclampsia, severe preeclampsia, and fetal growth restriction when low dose aspirin was initiated at >16weeks. Women who are at high risk for those outcomes should be identified in early pregnancy.[10]

In another study, early vs late administration of lowdose aspirin was compared on the risk of perinatal death and adverse perinatal outcome. When compared with controls, lowdose aspirin started at 16 weeks gestation compared with lowdose aspirin started at >16 weeks gestation was associated with a greater reduction of perinatal death, preeclampsia, severe preeclampsia, fetal growth restriction and preterm birth. So, the study has concluded that Lowdose aspirin initiated at 16 weeks of gestation is associated with a greater reduction of perinatal death and other adverse perinatal outcomes than when initiated at >16 weeks.[11]

Conclusion

It is concluded that the frequency of preeclampsia was very low among high risk females after having antiplatelet therapy in first trimester. Hence, in future by adding antiplatelet therapy in such females presenting with underlying conditions may be prevented from preeclampsia. After reducing the incidence of preeclampsia we may have better fetal and maternal outcome.

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Authors Contribution

S.I.M, B.S, S.A: Conceptualization of Project, Literature Search, Drafting, Revision

S.A, B.S: Data Collection, Statistical Analysis, Writing of Manuscript