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Research Article

# Role of Aspirin in PIH

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**Abstract**

Pregnancy induced Hypertension is one of the complications of pregnancy.PIH is related to imbalance between prostacycline and thromboxane A2. The platelet inhibitors have a potent prophylactic effect in it. Aspirin in low doses is a potent inhibitor of platelet aggregation. Cases which suggestive to PIH have introduced low doses Aspirin at different terms of pregnancy to observe the changes in various parameters during pregnancy. It is observed that time of introduction of low dose Aspirin in pregnancy is significant. There is significant reduction in development of HT when low dose Aspirin is started at 12$^{th}$ week of pregnancy, while less effect if low dose Aspirin is stared after 12 weeks of pregnancy.

**Keywords:** Aspirin, Pregnancy induced Hypertension, Thromboxane A2, Platelets

## Introduction

HT is one of the commonest complication of pregnancy and is common cause of fetal and maternal mortality and morbidity.[1] There are several types of hypertensive disorders during pregnancy, namely – PIH(Pregnancy induced hypertension ), EH( essential HT) with pregnancy and various other organic causes of HT.[2] Pre-eclampsia is a multisystem disorder usually associated with raised blood pressure and protienuria.[2] In case of sever pre-eclempsia there may be wide spread thrombotic lesions affecting the placenta. Lowering of platelet count and increase in fibrin degradation products are seen to precede signs of pre-eclampsia.(($PGI_2$) Prostacycline is the most potent endogenous inhibitor of platelet aggregation . It is synthesized from intact vascular endothelial cells. Direct antagonist to prostacyclin is thromboxane A2. It is synthesized in platelets from Arachedonic acid. The disease process of PIH is delicately poised on a balance between prostacyclin and thromboxane A2. A slight excess of thromboxan A2 relative to prostacyclin is enough to initiate the pathological events leading to pre-eclampsia.[6]

Prevention of this dreadful condition calls for efficient prophylaxis apart from routine therapy. Attempts have been made to down the synthesis of thromboxaneA2. Since thromboxane A2 is a cyclooxygenase , product of arachedonic acid , procedure have been framed to block the enzyme cyclooxygenase. Thus platelet inhibitors have a potent prophylactic effect. Aspirin is an effective inhibitor of platelet aggregation and effective in prevention of development of PIH.[4] It blocks the enzyme cyclooxygenase without causing significant disturbance to the synthesis of prostacycline. Regular intake of antiplatelet aggregating agents like aspirin protect the mother from development of HT and pre-eclampsia. The fetus seems to be benefited from the normal placental blood flow leading to increased birth weight, decreased

prematurity and its associated fetal morbidity and mortality.[4]

In view of the development of serious complications of PIH and possible role of judicious use of low dose aspirin in its prevention and favorable outcomes, the present study is under taken to apprise the following :

1. Incidence of hypertensive disorders during pregnancy and their various types
2. Response of various types of hypertension in pregnancy with low dose of aspirin

## Material and Methods

This study is taken among the cases attended the antenatal outpatient department and also cases admitted in the obsteretic unit of the District Hospital , Siliguri, Darjeeling, during the period from may 2013 to Apr 2014 .

Cases with past history suggestive of hypertensive disorders and/ or its complications and cases who are identified as prone to develop HT during the course of pregnancy (hypothyroid, diabetic mother and family history of HT) are taken in this study.

The cases are randomly allocated in to one of the two groups A and B. Patients in group A are administered 75mg aspirin once daily while group B act as control.

Selection of cases: Both groups comprised of booked and unbooked (cases seen for the first time in mid and late pregnancy) cases. In the booked cases roll over test was under taken to identify the group of cases who are prone to develop PIH. Multigravida with HT during this pregnancy and / or past obsteretic history suggestive of hypertensive disorders were taken in this study.

The roll over test was done at 24 – 26 weeks of pregnancy. The cases who have positive results were taken in this study. Patients were labeled hypertensive when the systolic BP was 140 mmHg or more, or diastolic BP was 90 mmHg or more. Also cases with an increment of 30 mmHg or more of systolic BP 15mmHg or more of diastolic BP from the BP in first trimester were also taken in this study.

In all cases initially clinical evaluation were under taken , namely identification (age, parity, gravida )social history , history of present pregnancy events and incidence during this pregnancy, menstrual history and family history were thoroughly evaluated.

While evaluating the events during pregnancy , specific problems like swelling of legs , scanty urine , headache , visual disturbances were recorded, if any obsteretic history was scanned with regards to the complications, during pregnancy , namely HT, IUGR, preterm labour , intrapartam problems of delivery , pueperium and the condition of the new born, birth weight and neonatal problems.

A detailed general examination was made regarding ,built , nutrition , height , weight , presence of anemia , cyanosis , jaundice , and neck veins , neck glands, thyroid swelling, if any were recorded . Examination of pulse, respiratory rate, temperature and BP were recorded. The condition of heart, lung, liver, spleen and kidneys were assessed.

A detailed obsteretical examination was carried out at each antenatal visit and height of fundus (symphysis – fundus distance in cm), abdominal girth at umbilicus were recorded.

Subsequently routine investigations like Hb%, blood group(ABO), Rh typing, test for VDRL (serology) , blood sugar (2 hours post parandial), bleeding time, clotting time , platelet count , were done and repeated after 36 weeks of gestation .Blood urea, creatinine and uric acid were estimated.

Urine was examined for protein and also in a few selected cases total protein estimation was advised. USG examinations were done routinely for fetal profile at 16-24 weeks of frequency.

With regards to management during pregnancy, apart from the specific treatment program, other routine medication were under taken . In few selected cases of sever HT, antihypertensive drugs were use . FHS were recorded with stethoscope and in selected cases with Doppler method. During labour intrapartum fetal and maternal monitoring were undertaken. Details of labour were recorded.

The babies were examined for any congenital anomalies and also presence of any drug effect. Babies were assessed by Apgar scoring at 1 and 5 minutes after birth.Weight of the babies were also recorded.

**Observations:**

The cases were randomly placed in one of the two groups:

Group A – Those who were given 75mg Aspirin orally daily

Group B – Control group receiving only routine iron and calcium or folic acid supplementation

**Table -1** Incidence of PIH in susceptible group

| Group of patient | No. of cases | PIH developed in | No. of cases with EH |
|---|---|---|---|
| A | 150 | 41 (27.33%) | 14 |
| B | 150 | 93 (62%) | 15 |

**Table -2**Distribution of type of hypertensive disorders in pregnancy in study group:

| Type of Hypertension | No. of cases | Relative incidence |
|---|---|---|
| Pregnancy induced hypertension (PIH) | 134 | 82.08% |
| Essential hypertension (EH)<br>(with or without superimposed PIH) | 29 | 17.02% |

**Table -3** Relationship of hypertensive disorders in pregnancy with age:

| Age ( in yrs) | PIH | EH |
|---|---|---|
| 15 – 25 | 63 ( 46.42%) | 10 (33.33%) |
| 26 - 35 | 71 (53.58% ) | 19 (66.67%) |

**Table -4**Time of appearance of Hypertension:

| Weeks of gestation | PIH (134) | EH (29) |
|---|---|---|
| Upto 20 wks | 0 | 9 |
| 21 – 28 wks | 18 (13.09%) | X |
| 29 – 32 wks | 59 (44.04%) | X |
| 33 - term | 57 (42.87%) | X |

**Table-5** Outcome of pregnancy where prophylactic low dose Aspirin were administered before and after 12 weeks

| Pregnancy complications | Prophylactic low dose Aspirin administered before 12 weeks | Prophylactic low dose Aspirin administered after 12 weeks | P-Value |
|---|---|---|---|
| | N = 36 | N=114 | |
| Mild HT | 18 (50%) | | 0.702 |
| Moderate HT | 12 (33.33%) | | 0.498 |
| Sever HT | 0 | | <0.001 |
| IUGR | 0 | | 0.022 |
| IUD | 0 | | 0.336 |
| Preterm labour | 0 | | 0.336 |
| 1$^{st}$ week death | 0 | | 0.336 |

**Table – 8** Time of appearance of proteinuria

| Weeks of gestation | PIH (134) | EH(29) |
|---|---|---|
| Upto 20 wks | 0 | X |
| 21 – 28wks | 5 (3.57%) | 1 (11.11%) |
| 29 – 32 wks | 40 (29.76%) | 2 (22.22%) |
| 33 - term | 89 (66.67%) | X |

Further it was revealed from our study that the majority of the cases of PIH (53.6%) had mild proteinuria i.e. one plus (+) , 37 cases (44.04%) had moderate proteinuria. Incidence of massive proteinuria was found in one each in PIH and EH group.

**Table – 9** Study of Blood Urea level in hypertensive disorders :

| Nature of cases | Total | Below 20 mg% | 21 – 30 mg% | 30 -40 mg% |
|---|---|---|---|---|
| PIH | 134 | 28 (21.42%) | 85 (63.09%) | 21 (15.49%) |
| EH | 29 | 6 (22.22%) | 23 (77.78%) | x |

It is evident from the table that the blood urea level are increased in all types of hypertension in pregnancy. In 53 cases out of 84 (63.09%) PIH cases and 7 out of 9 (77.78%) EH cases blood urea level was found to be raised in the range of 21 – 30 mg%. Serum uric acid level were studied in 56 cases , 49 cases with PIH , 7 cases with EH. It was evident that serum uric acid levels were elevated significantly in 30 out of 49 cases (61.22%) of PIH and 5 out of 7 cases (71.42%) of EH.

**Table -10**Table showing time of initiation of therapy with Tab. Aspirin 75 mg OD orally:

| Time of initiation in wks of gestation | 12 weeks | 12 – 20 wks | 21 – 28wks | 29wks – term |
|---|---|---|---|---|
| Group – A (Aspirin) | 12 | 12 | 13 | 13 |

**Table – 11** Study of platelet count while on antiplatelet aggregating agent :

| Type of Hypertensive disease | No. of cases with reduction in platelet count | |
|---|---|---|
| | Group – A Aspirin (50) | Group – B Control (50) |
| PIH | 5 | 15 |
| EH | 1 | 2 |

Platelet count was taken to be reduced when it was below 2,00,000/Cu mm. Using such a parameter , it was found from table that 6 out of 50 cases (125)in Group A had low ptatelet count at term .It was also found that 17 patient in Group B (34%) developed low platelet count , accounting for platelet consumption when these drugs were not used I.e. control study.

## Results

In this study the incidence of PIH was 27.33% in patients taking low dose Aspirin and 62% in those not taking Aspirin in susceptible patients, which was statistically significant. Incidence of development of PIH was statistically significant in first pregnancy and gradually decreases in further pregnancies. There was no significant changes seen in platelet counts after administration of Aspirin. There was statistical significant decrease in incidence of sever HT in cases Aspirin administered before 12 weeks of pregnancy.

## Discussion

The results of this systemic study demonstrates a major beneficial effect of early onset of low dose

Aspirin in having the overall risk of preeclampsia especially in sever HT whose relative risk was statistically significantly reduced . However the use of Aspirin was not associated with a significant reduction in relative risk of mild HT. Though the effect of low dose Aspirin on moderate HT is not statistically significant but 31.57% reduction has been found. The difference in effectiveness of early onset low dose Aspirin in the prevention of sever HT but not of mild HT is that the pathophysiology of the two conditions is different and only the former is susceptible to the effect of aspirin.[4]

It has been seen that the complications related to HT has also been reduced, there is supportive evidence from Doppler Ultrasound studies that in a high proportion of cases of sever HT with associated FGR, unlike cases of mild HT without FGR , impedance to flow in the uterine arteries is increased.[3] Such increased impedance to flow is thought to be a consequence of inadequate trophoblastic invasion of the material spiral arteries and their conversion from narrow muscular vessels to wide nonvascular channels.[8]

Although the cause of preeclampsia is unknown, it is primarily a placental disorder. During implantation , deficient trophoblast invasion of the maternal spiral arteries leads to under perfusion of the uteroplacental circulation and placental ischemia .The resulting placental damage is thought to be responsible for the release of , as yet unknown , factors in to the maternal circulation , which then alter endothelial cell function and cause widespread circulatory changes.[7]Women with preeclampsia have deficient intravascular production of prostacycline, a vasodilator, and excessive production of thromboxane, a vasoconstrictor and platelet agonist. The potential antiplatelet effect of aspirin derives from inhibition of the platelet production of thromboxane.[9] Early trials of low dose aspirin for preventing and treating preeclampsia were suggested a considerable reduction in risk of preeclampsia .There is comparable reduction in more substantive outcomes , such as perinatal death and IUGR.[2]

According to present study early introduction of low dose Aspirin in susceptible cases of pregnancy is prophylactic to development of pregnancy induced hypertension and other secondary complications of PIH.

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