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Original Article

Role of Aspirin in Pregnancy with High Gestosis Score and Outcome

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Abstract

Background: *Preeclampsia and eclampsia are the second and third most common causes of maternal morbidity and mortality worldwide. Hypertensive disorders in pregnancy gestosis score (HDP-Gestosis score) was devised in India by Dr. Gorakh Mandrupkar with modifications by a committee is being used for the effective screening and prediction of preeclampsia. High score carries almost 83% sensitivity and 98% specificity for predicting the development of preeclampsia. Acetylsalicylic acid (Aspirin) demonstrates inhibitory effects on Cyclooxygenases (COX) leading to decrease synthesis of prostaglandins and thromboxane-A2 resulting inhibition of both inflammation and platelet aggregation which reduces the risk of developing hypertension and preeclampsia. The purpose of the study to observe the outcome of aspirin use in patients with high gestosis score.*

Materials and methods: *This descriptive observational study in a population 250 pregnant women with high gestosis score (>=3) from January 2021 to December 2022 in the Department of Obstetrics and Gynaecology of Chattagram Maa-O-Shishu Hospital Medical College. But at the end of the study period only 100 eligible candidates were taken for analysis of results, because 150 cases excluded due to denying to further follow up and termination of pregnancy were done in other centres. After getting an eligible patient through inclusion and exclusion criteria, informed consent was obtained describing the objectives and nature of the study. Demographic details were taken by means of case record form. Details of clinical data, investigation profile including abdominal sonography, biochemical parameters were recorded. Privacy and confidentiality was explained to the patient and maintained. Pregnant mother with high gestosis score were given Tablet Aspirin 75mg / 150mg (According to BMI) daily, during their first Ante-Natal Check-up (ANC) from 12 weeks to 32 weeks. Regular follow up (Minimum 4) was ensured. Data from admitted patient, follow up, termination, mood of delivery, feto maternal outcome up to discharge. Data were analyzed by percentage.*

Results: *Of the 12973 obstetric patients 1396 (10.76%) were presented with hypertensive disorders and among them 100 patients with high Gestosis score were included in our study as they successfully completed the follow up schedule (>4 visit), took regular dosage of Aspirin and termination of pregnancy with postpartum care was taken in our institute. In our study the mean age was found 28.69 years with mean BMI of 23.5 kg/m^2. 10.76% of admitted obstetric patients presented with hypertensive disorders of pregnancy. 69% mother ē in 20-35 years and 7% under 19 years and 24% more than 35 years. 75% were multipara ē 65% had LSCS. 79% were patient ē in normal BMI 14% Obese. Risk factor 41% pregnant women gestational hypertension, 39% GDM, 27% hypothyroid and others. 63% women ē high gestosis score started Tablet Aspirin within 20 weeks of gestation. 84% women had uneventful outcome ē Tablet Aspirin but 11% developed preeclampsia, 5% maternal*

nearmiss (2 LVF, 2 PPH, 1 PPE). 74% women had term delivery only 20% had preterm termination. 74% baby ē good APGER SCORE, LBW were 16% and VLBW were 7%, 2% still birth.

Conclusion: *HDP-gestosis score is a novel marker to predict the development of preeclampsia with high diagnostic accuracy. HDP-gestosis scoring and Aspirin intake for preeclampsia, have remarkable impacts on maternal and fetal health and well-being.*

Key words: Aspirin; HDP-gestosis score; Preeclampsia.

INTRODUCTION

Preeclampsia is a pregnancy-specific multi organ disease that occurs after the 20th week of pregnancy and is defined as the new onset of hypertension (Systolic Blood Pressure [SBP] > 140 mm Hg or Diastolic Blood Pressure [DBP] > 90 mm Hg, on two occasions at least 4 hours apart) in a person with previously normal blood pressure, together with additional specified signs or symptoms.[1,2] In the absence of proteinuria, preeclampsia is diagnosed when hypertension is accompanied by any of the following signs or symptoms: thrombocytopenia, impaired liver function as indicated by elevated blood concentrations of liver enzymes and severe persistent right upper quadrant or epigastric pain unresponsive to medication, renal insufficiency, pulmonary edema, new-onset headache unresponsive to medication; or visual disturbances.[1] Preeclampsia increases the risk of intrauterine growth restriction, small for gestational age, low birth weight, preterm birth, placental abruption, stillbirth and neonatal death.[2] Preeclampsia and eclampsia are the second and third most common causes of maternal morbidity and mortality worldwide.[3-5] Maternal mortality in Bangladesh 24% due to preeclampsia and eclampsia. The majority of preeclampsia cases occur after 34 weeks, but perinatal morbidity and mortality are greatest for early onset disease.[6] Due to the fact that the only effective treatment for preeclampsia is delivery, the condition is a leading cause of medically induced preterm birth and low birth weight. It has been estimated that preeclampsia contributes to 6 percent of preterm births and 19 percent of medically indicated preterm births.[7] Preeclampsia is associated with increased risk of maternal chronic hypertension and cardiovascular disease later in life, including congestive heart failure, myocardial infarction, and stroke.[8,9] The risk appears to be greatest among women who have experienced preeclampsia in more than one pregnancy required preterm delivery or had a pregnancy complicated by fetal growth restriction.[10,11] The development of preeclampsia is usually presented as involving at least two stages—the placental stage and the maternal stage. The placental stage involves abnormal placentation, which contributes to early-onset preeclampsia (Delivery <34 weeks gestation) and/or placental microvillus overcrowding, which develops with advancing pregnancy and is thought to contribute to late-onset of preeclampsia.[12,13] The consequence of these changes is reduced placental perfusion, leading to hypoxia, placental ischemia, oxidative stress, and ultimately the release of damaging factors (i.e Cellular debris, oxidized lipids, antiangiogenic factors, soluble endoglin) into the maternal blood stream.[14-16] The second, "maternal" stage involves the development of systemic maternal sequelae resulting from placental dysfunction.[14] Placental damage leads to activation of platelets and the maternal clotting system and a systemic inflammatory response.[17,16] Changes in the renin-angiotensinaldosterone system and increased sensitivity of blood vessels to contractile agents result in vasoconstriction.[17] Reduced perfusion, resulting from vasoconstriction, vascular occlusion by microthrombi, reduced vascular volume from leaking of fluid from the intravascular compartment, and vascular inflammation affect virtually every maternal organ in a women with preeclampsia.[14,17] Placental perfusion abnormalities may also affect the fetus, leading to increased-risk of fetal growth restriction among women with preeclampsia. Currently, the World Health Organization recommends daily calcium supplementation (1.5-2.0g oral elemental calcium) for pregnant women with low dietary calcium intake to reduce the risk of preeclampsia, whereas ACOG does not. Medications such as heparin, metformin, sildenafil and statins, nutritional supplements and dietary modifications have been or are being explored for the prevention of preeclampsia, but, aside from calcium, none have been identified as efficacious.[18,19-24] Acetylsalicylic acid (Aspirin) demonstrates inhibitory effects on Cyclooxygenases (COX) leading to shifts in the synthesis of prostacyclin and thromboxane A2[25] This results in a two-fold action, reducing both platelet aggregation and vasoconstriction. Aspirin also leads to reduction in the synthesis of other prostaglandins, such as PGE2, which are involved with inflammation, contributing to aspirin's effect as an anti-inflammatory agent.[26] The inhibition of platelet aggregation and reduced vasoconstriction, as well as aspirin's anti-inflammatory effects are thought to provide the basis by which aspirin administration may reduce the risk of development of gestational hypertension and preeclampsia.[27,25,28-29] Evidence from a moderate-sized body of trial evidence that includes several large trials has established that aspirin modestly reduces the risk of preeclampsia in increased-risk populations.[30-32] Most recently, a large multisite trial conducted in low income and middle income countries reported a statistically significant benefit of low dose aspirin use for prevention of preterm birth and perinatal mortality among nulliparous individuals.[33]

A simple risk model named HDP-gestosis score has been devised by Dr. Gorakh Mandrupkar with further modifications by committee including "Dr. Sanjay Gupte, Dr. Suchitra Pandit, Dr. Alpesh Gandhi and Dr. Girija Wagh" for effective screening and prediction of Preeclampsia.[34] A total score is obtained from detailed history and examination of the woman. According to

HDP-Gestosis score the risk of development of preeclampsia are: Mild risk (Score of 1), Moderate risk (Score of 2) and High risk (Score of equal to or more than ≥ 3). The scoring parameters are as follows:-

Risk factor Score :

Age>35 years □	1
Age<19 years □	1
Maternal anaemia □	1
Obesity (BMI>30) □	1
Primigravida□	1
Short duration of sperm exposure (Cohabitation) □	1
Woman born as small for gestational age □	1
Family history of cardiovascular disease□	1
Polycystic ovary syndrome □	1
Inter pregnancy interval more than 7 years □	1
Conceived with Assisted Reproductive (IVF/ ICSI) Treatment □	1
MAP>85 mm of Hg □	1
Chronic vascular disease (Dyslipidemia) □	1
Excessive weight gain during pregnancy □	1
Maternal hypothyroidism □	2
Family history of preeclampsia □	2
Gestational diabetes mellitus □	2
Obesity (BMI>35 kg/m2) □	2
Multifetal pregnancy □	2
Hypertensive disease during previous pregnancy □	2
Pregestational diabetes mellitus □	3
Chronic hypertension □	3
Mental disorders □	3
Inherited/Acquired Thrombophilia □	3
Maternal chronic kidney disease □	3
Autoimmune disease (SLE/APLAS/RA) □	3
Pregnancy with Assisted Reproductive (OD or Surrogacy) □	3
Treatment for hypertensive disease of pregnancy □	3

High gestosis score (>=3) carries sensitivity, specificity, PPV and NPV of 83.1%, 97.51%, 85.51%, and 97.03%, respectively, for predicting the development of preeclampsia.[35] It seems to be a reliable marker to detect the development of preeclampsia and allowing obstetricians to take appropriate management for both mother and fetus. The purpose of the study to observe the outcome of aspirin use in patients with high gestosis score.

MATERIALS AND METHODS

This descriptive observational study in a population 250 pregnant women with high gestosis score (≥=3) from January 2021 to December 2022 in the Department of Obstetrics and Gynaecology of Chattagram Maa-O-Shishu Hospital Medical College. But at the end of the study period only 100 eligible candidates were taken for analysis of results, because 150 cases excluded due to denying to further follow up and termination of pregnancy were done in other centres. After getting an eligible patient through inclusion and exclusion criteria, informed consent was obtained describing the objectives and nature of the study. Demographic details were taken by means of case record form. Details of clinical data, investigation profile including abdominal sonography, biochemical parameters were recorded. Privacy and confidentiality was explained to the patient and maintained. Pregnant mother with high gestosis score were given Tablet Aspirin 75mg / 150mg (According to BMI) daily, during their first Ante-Natal Check-up (ANC) from 12 weeks to 32 weeks. Regular follow up (Minimum 4) was ensured. Admitted patient follow up, termination, mood of delivery, feto maternal outcome up to discharge. Data was analyzed by percentage.

RESULTS

Of the 12973 obstetric patients 1396 (10.76%) were presented with hypertensive disorders and among them 100 patients with high Gestosis score were included in our study as they successfully completed the follow up schedule (>4 visit), took regular dosage of Aspirin and termination of pregnancy with postpartum care was taken in our institute.

In our study the mean age was found 28.69 years with mean BMI of 23.5 kg/m^2. 10.76% of admitted obstetric patients presented with hypertensive disorders of pregnancy.

Table I shows 69% mother ē in 20-35 years and 7% under 19 years and 24% more than 35 years. 75% were multipara ē 65% had LSCS. 79% were patient ē in normal BMI ē 14% Obese. Table II shows Risk factor 41% pregnant women ē gestational hypertension, 39% GDM, 27% hypothyroid and others. 63% women high gestosis score started ē Tablet Aspirin within 20 weeks of gestation (Table III). 84% women had uneventful outcome ē Tablet Aspirin but 11% developed preeclampsia, 5% maternal nearmiss (2 LVF, 2 PPH, 1 PPE) (Table IV). Table V shows 74% women had term delivery only 20% had preterm termination. 74% baby ē good APGER SCORE, LBW were 16% and VLBW were 7%, 2% still birth (Table VI).

Table I Demography of respondent

Variables□	Ranges□	Numbers□	Percentage
Age (Years)□	<19□	07□	07
□	20-35□	69□	69
□	>35□	24□	24
Parity□	Primigravida□	25□	25
□	Multigravida□	75□	75
BMI (kg/m^2)□	18-24□	79□	79
□	25-29.9□	14□	14
□	30-34.9□	5□	5
□	>35□	2□	2
Mode of Delivery□	Vaginal□	35□	35
□	LUCS□	65□	65

Table II Pregnancy with Risk factors

Risk factors	Number	%
Anaemia	25	25
Family history of cardiovascular disease	18	18
Gestational Diabetes Mellitus (GDM)	39	39
Diabetes mellitus	19	19
Chronic hypertension	23	23
Gestational hypertension	41	41
Previous history of Preeclampsia	19	19
Hypothyroidism	27	27
Hyperthyroidism	04	04
Polycystic Ovary Syndrome (PCOS)	07	07
Autoimmune disease	01	01
Heart disease	01	01
Kidney disease	01	01
Mental disorders	01	01
Pregnancy with assisted reproduction	00	00
Previous history of IUD	02	02

Table III Gestational Age of starting Aspirin

	Gestational Age of starting Aspirin	
Weeks	Numbers	%
12-20	63	63
20-28	31	31
>28	06	06

Table IV Maternal Outcome

Maternal Outcome	Numbers	%
Preeclampsia	11	11
PPH	02	02
Postpartum eclampsia	01	01
LVF	02	02
Uneventful	84	84
Total	100	100

Table V Termination of pregnancy

Weeks	Numbers	%
<34 weeks	07	07
34-36 weeks	13	13
37-40 weeks	74	74
>40 weeks	06	06
Total	100	100

Table VI Fetal Outcome

Fetal Outcome	Numbers	%
Healthy	74	74
LBW	16	16
VLBW	07	07
IUD	01	01
Still birth	02	02
Total	100	100

DISCUSSION

Globally, about 12% of mothers die only from preeclampsia.[36] As estimated by WHO, the occurrence of preeclampsia is seven times higher in developing countries compared to developed countries.[37] The prevalence of preeclampsia ranges between 1.8 and 16.7% in developing countries.[38] In our study 10.76% of admitted obstetric patients presented with hypertensive disorders of pregnancy. This finding falls in the lower side of the range. As our study place is located in an urban area with available transport facilities and specialist consultation this finding may not correlate with other rural or less developed area of our country. A study conducted in our neighboring country India reported the prevalence of preeclampsia about 28% with a variation in the prevalence across the states or regions.[39]

The risk of developing preeclampsia is highest amongst women under 20 years of age, but women 35 years of age also have an increased risk of developing preeclampsia.[40] In our study 7% mother under 20 years and 24% mother more than 35 years were with high gestosis score but only 11% developed preeclampsia without adverse maternal outcome. As our study place is a metropolitan area the rate of childhood marriage and early conception is lower.

Preeclampsia usually occurs in primigravida but in our study with aspirin intake only 11% patients developed preeclampsia of whom 9.3% mother were multigravida. The frequency of preeclampsia in multigravida women was 19.8% at Shaikh Zaid Women Hospital Larkana, Pakistan.[41]

A strong direct correlation was found between an increasing body mass index (BMI) and the risk of developing preeclampsia and pregnancy induced hypertension.[42] The adjusted risk of developing preeclampsia doubled for overweight mothers with a BMI of 26 kg/m^2 and almost tripled for obese mothers with a BMI of 30 kg/m^2.[43] In our study 14% overweight mother (BMI ≥ 26 kg/m^2) and 7% obese (≥30 BMI) but only 11% developed preeclampsia despite application of Aspirin. Early termination of pregnancy (Before 36 weeks in 20% mother) was done due to placental praevia, uncontrolled hypertension with LVF, preterm labour, impending signs of eclampsia, scar tenderness, etc. Very low birth weight baby (7%) was found not for preeclampsia but due to PROM, preterm delivery, low socioeconomic status, poor nutrition and food habit of the mother. There was one IUD case due to postdated pregnancy and two still birth cases died in home trial having obstructed labour. It is reassuring that prophylactic use of aspirin has no negative effect on perinatal mortality.[44]

LIMITATION

Multicenter research with increase number of patients is needed to implement Aspirin as a routine practice. The safety margin of 150 mg Tablet Aspirin is not yet established.

CONCLUSION

HDP-gestosis score is a novel marker to predict the development of preeclampsia with high diagnostic accuracy. HDP-gestosis scoring and Aspirin intake for preeclampsia, have remarkable impacts on maternal and fetal health and well-being.

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DISCLOSURE

All the authors declared no competing interest.

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