Research Article

Study of relationship between pregnancy induced hypertension and homocysteine

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Abstract

Objective: To assess the homocysteine level in pregnancy induced hypertensive patient and also correlate levels of homocysteine in preeclampsia and pregnancy outcome. **Method:** It is a case control study conducted in antenatal ward at Government maternity hospital, Sultan Bazar. 100 subjects were recruited for study during antenatal period irrespective of gestational age and gravidae, during the year 2007-2008, were taken into the study.50 subjects were included those who fulfilled inclusion criteria**. Results:** Most of the patients are less than 20 years of age. Most of the patients are in second gravidae. Homocysteine levels are more with patient with second gravidae with diastolic blood pressure more than 100 mm of Hg and also showing significant proteinuria. High homocysteine level with preeclampsia patient have more preterm delivery rate with high caesarean section rate. It also shows some elevation in liver enzyme, in renal parameter and coagulopathy. In baby it was with abnormal non stress test. Most of the babies delivered are IUGR, LBW and preterm. **Conclusion:** Preeclampsia is a leading cause of maternal and fetal mortality and morbidity.The exact mechanism how Hyperhomocysteinemia promotes endothelial dysfunction remains unclear, but it involve both cytotoxic and oxidative stress mechanism to promote endothelial dysfunction in preeclampsia.Hyperhomocysteinemia has shown to be associated with number of complications in pregnancy. In the form of IUGR, preterm deliveries, low birth weight, repeated abortions, pregnancy induced hypertension and Abruptio placentae.
Keywords: hypertension and homocysteine.

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INTRODUCTION

Hypertensive disorders are among the commonest medical disorders during pregnancy and continue to be the major cause of maternal and perinatal morbidity and mortality worldwide. In developing countries they rank second only to anaemia with approximately 7-10% of all pregnancies being complicated by some form of hypertensive disease. Preeclampsia is a multisystem disorder of unknown aetiology, unique to pregnancy with onset after twenty weeks of gestation. Preeclampsia defined as persistent (lasting more than 6hours) 15mm of Hg rise in diastolic pressure or 30mmof Hg systolic pressure persistent blood pressure at least 140/90mmof Hg and a urinary proteinuria of 300mg /dl or more or a score of 1+or higher on a urine dipstick test. Hyperhomocysteinemia is an independent risk factor for cardio vascular diseases and obstetric problems. Preeclamptic patients tend to have higher plasma homocysteine levels. Homocysteinemia is associated with neural tube defects, recurrent abortions, IUGR, preterm

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deliveries, Abruptio placenta, IUD and DVT. Homocysteine is a sulphur containing amino acid, present in low micromole concentration in human blood. Inherited condition homocysteinuria is caused most frequently by complete deficiency of cystathione beta synthase.[1] Normal level of homocysteine is 5 to 15micromol/lit. level above 15micromol/lit is considered Hyperhomocysteinemia. During pregnancy the fall of homocysteine level is more during second trimester than first trimester. The mean homocysteine level during pregnancy.[2]

- 8-10 weeks of gestation age 5.6micromol/lit.
- 20- 28 weeks of gestation age 4.3 micrimol/lit.
- 36-42 weeks of gestation age 5.5 micromol /lit.

During second trimester homocysteine level fall is due to

1. High oestrogen level.
2. Haemodilution due to increase in blood volume.

High oestrogen level in pregnancy has protective effect on coronary heart disease by

a) Increased high density lipoprotein
b) Decrease in homocysteine level

AIM OF THE STUDY

1. To assess the level of homocysteine in preeclamptic patients.
2. To correlate levels of homocysteine in preeclampsia and pregnancy outcome.

MATERIAL AND METHODS

It is a case control study conducted in antenatal ward at Government maternity hospital, Sultan Bazar. 100 subjects were recruited for study during antenatal period irrespective of gestational age and gravidae, during the year 2007-2008 were taken into the study. 50 subjects were included those who fulfilled inclusion criteria.

Inclusion Criteria

- Hypertension
  Systolic blood pressure more than 140 mm of Hg.
  Diastolic blood pressure more than 90 mm of Hg.
- Proteinuria 1+ or 300mg/dl

Exclusion Criteria

- History of previous hypertension
- Known vitamin deficiency (folic acid, B12).
- Prior significant medical illness

Blood sample were obtained after overnight fasting period. Plasma was prepared from blood anticoagulated with ethyenediaminotetre-acetic acid. Sample collected from antecubital veins in supine position before any medication. Sample were divided into aliquots under sterile condition and stored at -80 degree centigrade until assay. Sample were centrifuged at 300rpm. Plasma total homocysteine level were measured by ELX 800 ELISA machine at 450 nm wave length using axis kits and result were recorded as micromol / lit. All the result are given as mean/ standard deviation $p< 0.05$ considered to be significant[3]

Plasma homocysteine level in PIH and pregnancy outcome

Total number of Patient: 100
Group a test: 50
Group b test control: 50

OBSERVATION AND RESULTS

Hyperhomocysteinemia in PIH

To correlate the association between plasma homocysteine in preeclamptic mother and its pregnancy outcome.

A total number of 100 patients were taken for the study.
50 Patients test (group- A)
50 Patients control (group- B)

Age: Most of the patients are in the age group < 20 years in test group compared to controls (table-1).

Table 1: Age distribution

Age group(years)	No. of patients in test	No. of patients in control
<20 YEARS	18	15
20-25 YEARS	14	12
25-30 YEARS	7	12
>30 YEARS	11	11

Gravidae: Study conducted in antenatal ward most of them are second gravidae 21(42%) , multigravidae 15 (30%) , and primigravidae 14 (28%). In both test and control group (table- 2) there is no significant correlation in terms of gravidae.

Table 2: Gravidae in group-A and group-B

Gravidae	Group-A	Group- B
Primi	14	19
Second	21	20
Three or more	15	11

Diastolic blood pressure and gravidae: Homocysteine level in relation to diastolic blood pressure in gravidae. Second gravidae with diastolic blood pressure above 100 mm of Hg had significant raised homocysteine level (50%). Compared to primigravidae (29%) and Multigravidae 21%. Where as in control group no significant change in homocysteine levels with DBP(table 3 and 4).

Table 3: Gravidae & diastolic blood pressure (mm of Hg) Group-A

Gravidae	<100 mm of Hg	100-110 mm of Hg	>110 mm of Hg
Primi	3	7	4
Second	4	10	7
Three or more	4	6	5

Table 4: Gravidae & diastolic blood pressure (mm of Hg) Group-B

Gravidae	< 100 mm of Hg	100-110 mm of Hg	>110 mm of Hg
Primi	18	1	-
Second	15	2	-
Three or more	10	3	-

Homocysteine and diastolic blood pressure: 70% of preeclamptic women had diastolic blood pressure above 100 mm of Hg in whom homocysteine level was above 14 micro mol / lit (p-0.01). (table 5 and 6).

Table 5: Homocystine and diastolic blood pressure (mm of Hg) Group-A

HOMOCYSTEINE(micro mol/lit)	DBP <100 Of mm of Hg	DBP >100 mm of Hg
< 14 micro mol/lit	2	5
>14 micro mol/lit	8	35

Table 6: Homocystine and diastolic blood pressure (mm of Hg) Group-B

HOMOCYSTEINE (micro mol/lit)	<100 mm of Hg	>100 mm of Hg
<14 micro mol/lit	44	1
>14 micro mol/ lit	2	3

Urine albumin: Homocysteine level in relation to urine albumin show significant effect. Second gravidae found to have high homocysteine level with significant proteinuria (p-0.04) (table 7).

Table 7: Homocystine and urine albumin

Homocysteine (micro mol/ lit)	Urine albumin< 2+	Urine albumin >2+
<14 micro mol/lit	12	6
>14 micro mol/lit	7	25

Gestational age and homocysteine levels: Preeclamptic women with high homocysteine level show preterm delivery between 34- 37 weeks of gestation. Where as in control group with normal homocysteine level had term delivery. (p- 0.01) (table-8).

Table 8: Homocysteine and gestational age

HOMOCYSTEINE(micro mol/lit)	<30 weeks	34-37 weeks	>37 weeks
<14 micro mol/ lit	1	4	5
> 14 micro mol/lit	6	21	12

Homocysteine levels in relation to mode of delivery: Most of the women with high homocysteine levels delivered by LSCS 54% compared to test, normal delivery was seen in control group. (table 9 and 10).

Table 9: Homocysteine and mode of delivery (Group-A)

HOMOCYSTEINE(micro mol/ lit)	NORMAL DELIVERY	L.S.C.S
<14 micro mol/lit	6	3
>14 micro mol/lit	15	26

Table 10: Homocysteine and mode of delivery (Group-B)

HOMOCYSTEINE (micro mol/lit)	NORMAL DELIVERY	L.S.C.S
<14 micro mol/lit	38	7
>14 micro mol/lit	2	3

Homocysteine and nst(non stress test): Women with high homocysteine levels had abnormal NST scores.(table 11).

Table 11: Homocysteine and NST

HOMOCYSTEINE(micro mol/ lit)	NST NORMAL	NST ABNORMAL
<14 micro mol/lit	6	10
>14 micro mol/lit	10	24

Relation of homocysteine level to organ dysfunction: Homocysteine has significant effect on vital organs. Mild elevation of renal parameters, liver enzymes and coagulopathy(table 12).

Table 12: Homocysteine and organ dysfunction in gravidae

Gravidae	Liver function test	Renal function	Coagulation
Primi	2	2	2
Second	9	7	5
Three or more	4	7	3

Homocysteine and effect on fetus: High homocysteine levels has significant effect on fetus and correlate with severity of disease. 34% IUGR, 22% Low birth weight and 22% preterm. The incidence of babies referred to NICU is 67% and 33% babies are normal. Compared to test, control group showed no significant maternal and fetal morbidity .(table 13).

Table 13: Homocysteine and pregnancy outcome

Homocysteine (micro mol/lit)	Preterm	Iugr	Lbw	Low apgar
14-20 micro mol/lit	3	12	6	2
>20 micro mol/lit	4	5	2	1

DISCUSSION

Hyperhomocysteinemia in PIH

In this case control study high plasma homocysteine was associated with increased risk of preeclampsia. Preeclampsia is a leading cause of maternal and fetal mortality and morbidity. Endothelial dysfunction has been proposed as a central feature of pathophysiology of preeclampsia, resulting in altered vascular integrity, activation of coagulation, decreased antioxidant activity and increased lipid perioxidase. Hyperhomocysteinemia is an independent risk factor for cardio vascular disease and obstetrics problem as first trimester – neural tube defects, recurrent spontaneous abortions, and in second trimester preeclampsia, abruption placentae and preterm

deliveries. Preeclamptic patients tent to have Hyperhomocysteinemia. In the study conducted by Rajkovic and colleague the incidence of preeclampsia is more in primigravidae with Hyperhomocysteinemia[4] In our study there is no significant association between preeclampsia and hypercysteinemia in primigravidae but showed high incidence of preeclampsia and Hyperhomocysteinemia in primigravidae but showed high incidence of preeclampsia in younger age group and second gravidae. Lind Bald and *et al* found direct relation between Hyperhomocysteinemia with preeclampsia.[5] Similar association were found in our study. Hogg and Vollset found, serum homocysteine levels decreasesduring normotensive pregnancy, parallel to fall in serum albumin concentration and no proteinuria but increased in preeclampsia[6,7] In our study significant association found with hyperhomocysteinemia and serum albumin showing proteinuria .patient with normal homocysteine level there is no proteinuria. According to study conducted by Rajkovic and Stein Emil *et al* found that hyperhomocystenemia associated with preterm delivery.[8, 9] our study showed similar association (22%), patient with hyperhomocystenemia landed in preterm labour. But Anderson in his study did not found any significant association[10] In study conducted by Jian Van most of them deliveredby LSCS not related to homocysteine level.[11] But in our study women delivered by LSCS had hyperhomocystenemia because most of them had PIH and developed fetal distress. In the study conducted by Leida *et al* had found correlation between homocysteine and IUGR.[12] In our study similar association found that hyperhomocystenemia have increased incidence of preeclampsia with poor pregnancy outcome. IUGR (34%), LBW (22%) and preterm delivery (22%). Among the delivered, babies referred to NICU because of low Apgar score due to due to fetal distress during labour. This is because hyperhomocysteinemia causes thrombosis in placenta blood vessel leading to ischemia and infraction of placenta. This reduces blood supply to fetus resulting in pathological reduction in their growth.

CONCLUSION

Preeclampsia is a disease unique to pregnancy that complicate from 5% to 7% of low risk pregnancy and 25% of high risk pregnancy. Hyperhomocysteinemia is an independent risk factor for coronary artery disease and peripheral vascular disease. The exact mechanism how Hyperhomocysteinemia promotes endothelial dysfunction remains unclear, but it involve both cytotoxic and oxidative stress mechanism to promote endothelial dysfunction in preeclampsia. Hyperhomocysteinemia has shown to be associated with number of complications in pregnancy. In the form of IUGR, preterm deliveries, low birth weight, repeated abortions, pregnancy induced hypertension and Abruptio placentae. In conclusion our studies shown those hyperhomocystenemia levels are significantly higher in pregnancy with preeclampsia. Our findings suggest that hyperhomocysteine has significant effect on pregnancy outcome.

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