

Association Between Serum Level of Homocysteine and Hypertensive Disorder of Pregnancy

Indu Gautam¹, Sushama²

¹Associate Professor, Department of Obstetrics and Gynaecology, SMS Medical College and Hospital, Jaipur, Rajasthan.

²Resident Doctor, Department of Obstetrics and Gynaecology, SMS Medical College and Hospital, Jaipur, Rajasthan.

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Corresponding author: Dr. Indu Gautam

Conflict of interest: Nil

Abstract:

Background: The homocysteine-mediated vascular changes are similar to those associated with preeclampsia, therefore, a hypothesis has been proposed that hyperhomocysteinemia may be associated with this condition. Homocysteine may provide the missing link in the etiology of preeclampsia.

Material & Methods: A sample size of Hundred patients 100 (50 patients per group) was calculated at 99% confidence interval at 5% acceptable margin of error by epi info software version 7.2. Enrollment of study participants was done from pregnant women >20 weeks of gestation admitted in Zenana Hospital, Department of Obstetrics and Gynaecology for delivery.

Results: In the present study, positive correlation between age of patient and serum homocysteine although not statistically significant. It also shows positive correlation between high blood pressure of women and serum homocysteine and it is statistically significant. There is a positive correlation of BMI which is also statistically significant. There is negative correlation of period of gestation with serum homocysteine and it is not significant statistically. There is positive correlation of birth weight of baby with serum homocysteine. The mean serum homocysteine level in women who underwent LSCS, is 15.45 ± 6.26 $\mu\text{mol/L}$ and in women who delivered by vaginal route is 13.11 ± 5.6 $\mu\text{mol/L}$. The mean serum homocysteine level is significantly higher in LSCS as compared to cases undergoing vaginal delivery.

Conclusion: We concluded from the present study that the serum homocysteine level is significantly elevated in women with hypertension and that serum homocysteine level has positive correlation with blood pressure.

Keywords: Hypertensive Disorder of Pregnancy, Serum Homocysteine Level, Preeclampsia.

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Introduction

Hypertension is an established and widespread medical condition during pregnancy [1]. It is the third imperative cause of death in pregnancy as well as perinatal and maternal morbidities. Blood pressure levels above 140/90 mmHg onwards with substantial proteinuria on 20 weeks of gestation and more having no

previous record of high arterial pressure and proteinuria define preeclampsia [2]. It has become common diagnosis in developed countries and is still increasing cause of fetal and maternal morbidity and mortality in the developing world [3]. Hyperhomocysteinemia could result from a genetic defect on enzyme participating in

homocysteine synthesis and metabolism or it could be because of deficiency of folic acid, vitamin B6, B12 [4]. Level of maternal serum homocysteine normally decreases with gestation, either due to a physiological response to the pregnancy, increase in estrogen, hemodilution from increased plasma volume, or increased demand for methionine by both the mother and fetus [5].

Elevated level of homocysteine is associated with number of placenta mediated diseases such as preeclampsia and several pregnancy complications like habitual abortion, placental abruption, thromboembolic events, neural tube defect, intrauterine fetal death and fetal growth restriction [6]. Although the exact incidence of preeclampsia is unknown, it has been reported to be approximately 5-8% [7].

The exact pathophysiological process of preeclampsia is not known, but currently, endothelial dysfunction is most popularized to a central pathophysiologic feature of preeclampsia, leading to altered vascular reactivity, loss of vascular integrity and activation of the coagulation cascade [7]. The homocysteine-mediated vascular changes are similar to those associated with preeclampsia, therefore, a hypothesis has been proposed that hyperhomocysteinemia may be associated this condition [8,9]. Homocysteine may provide the missing link in the etiology of preeclampsia [10]. Therefore, this study is conducted to determine any association between serum level of homocysteine and hypertensive disorder of pregnancy.

Materials & Methods

The present hospital based observational study was conducted in the department of Obstetrics and Gynaecology, SMS Medical College, Jaipur. The total duration of study was one year from March 2021 to February 2022. A sample size of Hundred patients 100 (50 patients per group) was calculated at 99% confidence interval at 5% acceptable margin of error by epi info

software version 7.2. Enrollment of study participants was done from pregnant women >20 weeks of gestation admitted in Zenana Hospital, Department of Obstetrics and Gynaecology for delivery. Institutional Ethics Committee Clearance was obtained before start of study and written and informed consent for the procedure was obtained from all the patients. Strict confidentiality was maintained with patient identity and data and not revealed, at any point of time.

Demographic data was collected about each participant; which were included age, height, weight, smoking habit, ethnicity and parity. Routine checkup was done including blood pressure. Based on inclusion and exclusion criteria patients were selected as a case if blood pressure $\geq 140/90$ mm of Hg (Group A) or control if blood pressure $\leq 140/90$ mm of Hg (Group B). All study participants were subjected for Complete blood count and ABO Rh group, urine analysis, serum bilirubin, SGOT, SGPT, Blood sugar, serum urea, uric acid and creatinine, serum electrolyte and Serum homocysteine along with coagulation profile and USG for fetal well-being.

Data were entered in the MS office 2010 spread sheet and Epi Info v7. Data analysis was carried out using SPSS v22. Qualitative data was expressed as percentage (%) and Pearson's chi square test was used to find out statistical differences between the study groups and sensitivity, specificity, positive predictive value and negative predictive value were calculated. If the expected cell count was < 5 in more than 20% of the cells then Fisher's exact test was used. All tests were done at alpha (level significance) of 5%; means a significant association present if p value was less than 0.05 and highly significant if p value less than 0.01.

Results

In the present study the we enrolled 100 (50 per group) pregnant women >20 weeks of gestation admitted in Zenana Hospital, Department of Obstetrics and Gynaecology

for delivery. The average age of women in this study is 25.43 years, with minimum age 20 years and maximum age 31 years in both groups. The average age of the women in group A is 25.34 years and in group B is 25.52 years. There is no statistically significant difference in mean age of both the groups. (P value >0.05). Maximum number of cases in both groups are multigravida, comprising 66% of the study

population. In maximum number of cases in group-A, gestational age is <37 weeks. The mean gestational age of group-A is 33.52, indicating that preterm deliveries are more in women with severe hypertension compared to group-B where it is 36.66. There is statistically significant difference in mean gestational age of both the groups. (Table 1)

Table 1: Distribution according to parameters in both the groups.

Parameters		Group A(n=50)	Group B(n=50)	Total
Age(years)	<=25	27 (54%)	25 (50%)	52 (52%)
	>25	23 (46%)	25 (50%)	48 (48%)
	Mean \pm SD	25.34 \pm 2.64	25.52 \pm 2.86	25.43 \pm 2.74
Gravida status	Primi gravida	18 (36%)	16 (32%)	34 (34%)
	Multi gravida	32 (64%)	34 (68%)	66 (66%)
Period of gestation	<37 weeks	47 (94%)	25 (50%)	72 (72%)
	>=37 weeks	3 (6%)	25 (50%)	28 (28%)
	Mean \pm SD	33.52 \pm 1.97	36.66 \pm 2.23	35.09 \pm 2.62

In the present study, mean systolic blood pressure in group A and group B is 161.8 mm of Hg and 119.6 mm of Hg respectively. The mean diastolic blood pressure in group A and group B is 107.64 mm of Hg and 77.42 mm of Hg respectively. There is statistically significant difference in mean blood pressure between both the groups (Table 2).

Table-3 shows mean serum homocysteine level in both the groups. The mean serum homocysteine level is 14.37 μ mol/L and 11.08 μ mol/L in group-A, group-B respectively. The independent t test indicated that mean serum homocysteine level is significantly higher in group A as compared to that in group B.

Table 2: Distribution according to blood pressure levels.

Blood pressure(mmHg)	Group A(n=50)	Group B(n=50)	Total	P value
Systolic blood pressure(mmHg)				
Mean ± SD	161.8 ± 18.48	119.6 ± 6.69	140.7 ± 25.32	<.0001
Range	140-200	110-130	110-200	
Diastolic blood pressure(mmHg)				
Mean ± SD	107.64 ± 12.65	77.42 ± 4.45	92.53 ± 17.88	<.0001
Range	90-130	70-81	70-130	

Table 3: Distribution according to serum homocysteine levels.

Serum homocysteine(μ mol/L)	Group A(n=50)	Group B(n=50)	Total	P value
Mean \pm SD	14.37 \pm 6.02	11.08 \pm 4.44	12.73 \pm 5.52	0.002
Range	6.22-28.27	5.72-18.48	5.72-28.27	

In the present study, Table 4 shows positive correlation between age of patient and

serum homocysteine although not statistically significant. It also shows

positive correlation between high blood pressure of women and serum homocysteine and it is statistically significant. There is a positive correlation of BMI which is also statistically significant. There is negative correlation of period of gestation with serum homocysteine and it is not significant statistically. There is positive correlation of

birth weight of baby with serum homocysteine. the mean serum homocysteine level in women who underwent LSCS, is $15.45 \pm 6.26 \mu\text{mol/L}$ and in women who delivered by vaginal route is $13.11 \pm 5.6 \mu\text{mol/L}$. The mean serum homocysteine level is significantly higher in LSCS as compared to cases undergoing vaginal delivery.

Table 4: Correlation of Serum homocysteine($\mu\text{mol/L}$) with various parameters in group A.

Variables	Age (y)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Body mass index (kg/m^2)	Period of gestation (in weeks)	Birth weight (kg)
Serum homocysteine($\mu\text{mol/L}$)						
Correlation coefficient	0.212	0.319	0.383	0.592	-0.120	0.002
P value	0.140	0.024	0.006	<0.0001	0.408	0.987

Discussion

The present study is conducted on 100 pregnant women who attending Zenana Hospital, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur from March 2021 to February 2022. They are divided into two groups; Group A: Pregnant women with blood pressure $\geq 140/90$ mm of Hg and Group B: Pregnant women with blood pressure $\leq 140/90$ mm of Hg. In the present study the average age of women is 25.43 years, with minimum age 20 years and maximum age 31 years in both the groups. The average age of the women in group A is 25.34 years and in group B is 25.52 years. Singh Urmila et al (2009) in their study found that, mean age of women in the normotensive group was 28.03 ± 3.84 years, whereas in study group I and II (mild and severe preeclampsia) it was 25.06 ± 2.80 and 25.67 ± 3.40 years respectively, which was not significant statistically [11].

In the Metin Ingec et al (2005) study, the mean age was in control group 26.4 ± 5.4 years, in mild preeclampsia group 25.2 ± 3.4 years and in severe preeclampsia group it was 24.8 ± 3.4 years, that was statistically not significant ($P > 0.07$) (12). The study of

Yardanur G et al (2011) showed that, the mean age was 29.4 ± 3.49 years in control group, 29.6 ± 4.72 years in mild preeclampsia group and 30.3 ± 5.2 years in severe preeclampsia group. There was statistically no significant difference in mean age of all three groups ($P > 0.05$) [12].

Maximum number of cases in both groups are multigravida, comprising 66% of the study population. The Metin Ingec et al (2005) study showed percentage of primiparous women in normotensive group, mild preeclamptic group and in severe preeclamptic group was 29.4%, 34.4% and 28.0% respectively [12]. Sharma V et al (2019) conduct a prospective randomized controlled clinical trial of 50 patients. Out of 50 patients, it was found that there were, 22(44%) cases were primigravida whereas 28(56%) cases were above primigravida [14].

In maximum number of cases in group-A, gestational age is < 37 weeks. The mean gestational age of group-A is 33.52, indicating that preterm deliveries are more in women with severe hypertension compared to group-B where it is 36.66. There is statistically significant difference

in mean gestational age of both the groups. In the Yardanur G et al (2011) study, the mean gestational age was in 37.5 weeks in normotensive group, 35.1 weeks in mild pre-eclampsia group and 32.5 weeks in severe pre-eclampsia group [13]. The Metin Ingc et al (2005)9 in their study found the mean gestational age at delivery was 38.2 week in normotensive group 37.0 week in mild pre-eclampsia group and 34.7 in severe pre-eclampsia group [12].

The mean systolic blood pressure in group A and group B is 161.8 mm of Hg and 119.6 mm of Hg respectively. The mean diastolic blood pressure in group A and group B is 107.64 mm of Hg and 77.42 mm of Hg respectively. There is statistically significant difference in mean blood pressure between both the groups. Sunita Ghike et al (2011) conducted a study on 60 pregnant women and she concluded that serum homocysteine levels were significantly elevated in women with PET compared with control group and strong correlation may exist between serum homocysteine levels and severity of pre-eclampsia [15]. Ganji V, Kafai[15] MR (2003) found systolic blood pressure was positively associated with serum homocysteine levels [16]. Sengwana D (2013) found the statistically significant relation between homocysteine and systolic and diastolic blood pressure[17].

The mean serum homocysteine level is 14.37 $\mu\text{mol/L}$ and 11.08 $\mu\text{mol/L}$ in group-A, group-B respectively. The independent t test indicated that mean serum homocysteine level is significantly higher in group A as compared to that in group B. Our observations are in consonance with Robert W. Power et al (1998) and Rajkovic, in which mean homocysteine levels were greater in pre-eclampsia than normotensive controls ($P < 0.01$). Powers RW et al (2001)71 found that total plasma homocysteine was significantly increased in women with pre-eclampsia compared to subjects with transient hypertension of pregnancy or normotensive pregnant

women (8.3 ± 2.5 mM versus $< 5.5 \pm 2.2$ and 5.4 ± 3.4 mM respectively, $P < 0.01$) [18]. Ezzatalsadat Haji et al (2012) studied that mean serum homocysteine level was significantly higher in women with severe preeclampsia than in control group ($P < 0.001$), but no significant difference between normal pregnant women and those with mild preeclampsia ($P = 0.12$) [19].

All women in group A are showing albumin in urine and in group B 6 women out of 50 have albumin in urine. There is statistically significant difference in urine albumin of both the groups. 54% women underwent LSCS in group A as compared to 20 % in group B. There is statistically significant difference in mode of delivery of both the groups. Mean neonatal birth weight in group A and group B is 2.32 kg and 2.81 kg respectively. There is statistically significant difference in birth weight of baby of both the groups.

Conclusion

We concluded from the present study that the serum homocysteine level is significantly elevated in women with hypertension and that serum homocysteine level has positive correlation with blood pressure. This study recommends that a multicentric study with large population is needed to support the hypothesis that hyperhomocysteinemia is associated with hypertension.

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