COMPARASION OF SERUM HOMOCYSTEINE LEVELS IN PRIMIGRAVIDAS DURING SECOND AND THIRD TRIMESTERS OF NORMAL PREGNANCY AND PREECLAMPSIA

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ABSTRACT

Objective: To determine and compare serum homocysteine (Hcy) levels in primigravidas in second and third trimesters of normal pregnancy and preeclampsia.

Study Design: Cross-sectional comparative study.

Place and Duration of Study: Study was conducted at department of Gynecology and Obstetrics, Lahore General Hospital, from June 2013 to May 2014.

Material and Methods: One hundred primigravida patients of normal pregnancy and preeclampsia of second and third trimester were evaluated in terms of parameters including blood pressure and Hcy. The subjects were further subdivided into four groups. Age of patients was ranging from 18 to 40 years.

Results: The age of selected hundred subjects ranged from 18 to 40 years, while the mean ± SD age was 25.92 ± 5.56 years. Systolic blood pressure ranged from 100 to 210 mmHg, (mean ± SD 136.3 ± 24.623 mmHg). The recorded diastolic blood pressure ranged from 70 to 130 mmHg, (mean ± SD 87.8 ± 15.736 mmHg). There was a significant difference in Hcy amongst pre-eclamptics and controls of 2nd and 3rd trimesters and also between controls of 2nd and 3rd trimesters and cases of both 2nd and 3rd trimesters (p<0.05).

Conclusion: There is a significant increase in serum Hcy levels in both second and third trimesters of pregnancies with preeclampsia as compared to controls.

Keywords: Homocysteine, Preeclampsia, Primigravidas.

INTRODUCTION

Hypertension is an established and wide-spread medical condition during pregnancy[1]. It is the third most imperative cause of death in pregnancy as well as perinatal and maternal mor-bidities[2]. Blood pressure serves as a biomarker for the disease hypertension[3]. It is the systolic blood pressure of 140 mmHg at least and diastolic blood pressure of 90 mmHg at least which defi-nes hypertension. Its development from 140/90 mmHg onwards with substantial proteinuria on 20 weeks of gestation and more having no pre-vious record of high arterial pressure and proteinuria define preeclampsia. It has become common diagnosis in developed countries and is still increasing cause of fetal and maternal morbidity and mortality in the developing world[4]. It affects 5% to 8% of pregnancies world-wide[5]. However, an autopsy data in Pakistan implies that up to 40% of women who die from postpartum hemorrhage (PPH) comp-lained of symptoms of preeclampsia e.g. head-ache, visual disturbances and abdominal pain or had seizures prior to the onset of their life-ending hemorr-hage[6]. Likewise, approximately 16% of the annual 2.6 million stillbirths occur in pregnancies complicated by pregnancy hypertension[7].

Homocysteine (Hcy) is a vital amino acid and it is related to pregnancy specific conditions and hypertensive disorders of pregnancy in nonpregnant adult population. Its levels in late first trimester (8 to 12 weeks) of pregnancy are significantly associated with prior pregnancy losses and hypertensive disorders of pregnancy, particularly in the second and third trimesters. Increased serum Hcy levels are also significantly associated with meconium stained amniotic fluid,

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oligohydramnios, and low birth weight[8]. It has a direct statistical correlation with the severity of hypertension and complication with preeclampsia and eclampsia. It can be considered as a reliable predictive marker for pregnancy induced hypertension. Hyperhomocysteinemia is a risk factor for endothelial dysfunction, vascular disease and complications like abruption, retinopathy, acute renal failure, cerebrovascular accident, disseminated intravascular coagulation, and shock. The levels also correlate with the severity of hypertension and complications with preeclampsia and eclampsia[9]. Normal plasma concentration of Hcy is ranged as 4-12 µmol/l while mean Hcy concentrations are 5.6 µmol/l at 8-16 weeks, 4.3µmol/l at 20-28 weeks, and 5.5µmol/l at 36-42 weeks of gestation[10,11].

This study was conducted not only to examine a possible relationship between Hcy levels and preeclampsia in Pakistani population in second and third trimesters of pregnancy but to find out cost effective way out of these morbid conditions which badly affect health of a mother and her children, household productivity, and national wealth.

PATIENTS AND METHODS

A cross-sectional comparative study was designed which was conducted at Lahore General Hospital, Lahore during June 2013 to May 2014. Hundred patients, aged 15 to 40 years were included in this study and they were further subdivided into four groups i.e. group I: 50 primigravidas having preeclampsia. Group Ia: 25 females with preeclampsia in second trimester of pregnancy. Group Ib: 25 females with preeclampsia in third trimester of pregnancy Group II: 50 controls are primigravidas with uncomplicated pregnancy. They were further subdivided into two groups. Group IIa: 25 normal controls in second trimester of pregnancy. Group IIb: 25 normal controls in third trimester of pregnancy[12]. Non-probability convenience sampling was used for data collection. Primigravida in second and third trimester of normotensive nonproteinuric pregnancy aged 15-40 years were included as controls while primigravida in second and third trimester aged 15-40 years with systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg on two occasions which are six hours apart after 20 weeks of pregnancy in a woman whom blood pressure was normal previously and proteinuria ≥ 0.3 gram in a 24-hours urine specimen were included as cases. The subjects with past history of hypertension, cardiovascular or renal diseases, diabetes mellitus, multiple pregnancy, acute and chronic liver diseases, and subjects on anti-folate drug therapy e.g. anti-epileptics, methotrexate were excluded from the study[13]. After taking informed consent from the patients fulfilling the inclusion criteria, samples were drawn and results were obtained. A specimen of 3 ml of blood was collected in disposable syringe from each subject by venepuncture under aseptic measures. The blood was allowed to clot in test tube and then centrifuged. Serum was separated and stored in serum cups at a temperature of -20°C for the assessment of serum Hcy (µmol/L) by Enzyme Immuno-assay (EIA). Data obtained was first entered in the Microsoft Excel sheet to generate data base which was exported in the SPSS version 19.0. Data were analyzed for description i.e. for continuous variables like age, blood pressure, and serum Hcy; mean ± standard deviation (± SD) was calculated. Data was presented in tables. A t-test was applied to observe group mean differences. Level of 5% (p<0.05) was used for significance testing and associations.

RESULTS

Age of Subjects of 2nd and 3rd Trimester

The age of selected controls ranged from 20 to 35 years with mean ± SD age of 27.40 ± 4.47 years in second trimester. While the age of cases with preeclampsia in second trimester ranged from 18 to 35 years with mean ± SD age of 25.36 ± 6.11 years. However, the age of selected controls in third trimester also ranged from 18 to 35 years with mean ± SD age of 24.92 ± 4.44 years and the age of cases with preeclampsia in third trimester

ranged from 18 to 40 years with mean ± SD age of 26.00 ± 6.85 years (table-I).

Comparison of blood pressure among cases and controls of 2nd and 3rd trimester

In controls of 2nd trimester, mean ± SD of systolic and diastolic blood pressures were115.20 ± 7.141and 72.80 ± 4.583 mmHg respectively. While in controls of 3rd trimester, the mean ± SD of systolic and diastolic blood pressures were 116.40 ± 9.188 mmHg and 75.60 ± 5.066 mmHg respectively. In cases of 2nd trimester, mean ± SD of systolic blood pressure was 149.20 ± 10.173 mmHg, while mean ± SD of diastolic blood pressure was 97.40 ± 8.431mmHg. However, in cases of 3rd trimester, mean ± SD of systolic and diastolic blood pressures were165.20 ± 18.511 mmHg and 105.40 ± 9.781 mmHg respectively (table-II).

Serum Homocysteine (HCY) of cases and controls in 2nd and 3rd Trimester

In 2nd trimester, mean ± SD of serum Hcy in controls was 4.85 ± 0.52(µmol/L) while mean ± SD of serum Hcy in preeclamptics was 7.39 ± 0.38(µmol/L). In 3rd trimester, mean ± SD of serum Hcy in controls was 6.39 ± 0.70 (µmol/L), while mean ± SD of serum Hcy in preeclamptics was 9.36 ± 0.25 (µmol/L) (table-III). There was a significant difference in Hcy amongst preeclamptics and controls of 2nd and 3rd trimesters and also between controls of 2nd and

Table-I: Age of subjects of 2nd and 3rd trimester.

Group in Respective Trimester	N	Minimum	Maximum	Age (mean ± SD years)
Controls in 2nd trimester	25	20	35	27.40 ± 4.47
Cases in 2nd trimester	25	18	35	25.36 ± 6.11
Controls in 3rd trimester	25	18	35	24.92 ± 4.44
Cases in 3rd trimester	25	18	40	26.00 ± 6.85

Table-II: Comparison of blood pressure among cases and controls of 2nd and 3rd trimester.

Group in respective trimester	Blood pressure (mm Hg)	Minimum	Maximum	Blood pressure (mm Hg)
mean ± SD				
Cases in second trimester	Systolic BP (mm Hg)	140	170	149.20 ± 10.173
	Diastolic BP (mm Hg)	90	120	97.40 ± 8.431
Control in second trimester	Systolic BP (mm Hg)	100	120	115.20 ± 7.141
	Diastolic BP (mm Hg)	70	80	72.80 ± 4.583
Cases in third trimester	Systolic BP (mm Hg)	140	210	165.20 ± 18.511
	Diastolic BP (mm Hg)	90	130	105.40 ± 9.781
Control in third trimester	Systolic BP (mm Hg)	100	140	116.40 ± 9.188
	Diastolic BP (mm Hg)	70	80	75.60 ± 5.066

Table-III: Mean ± SD of serum homocysteine (Hcy) of cases and controls in 2nd and 3rd trimester.

Group in respective trimester	Hcy (µmol/L) mean ± SD
Controls in 2nd trimester	4.85 ± 0.52
Cases in 2nd trimester	7.39 ± 0.38
Controls in 3rd trimester	6.39 ± 0.70
Cases in 3rd trimester	9.36 ± 0.25

Table-IV: Significant difference of serum homocysteine in cases and controls by t-test.

Group in respective trimester		*p*-value
Controls in 2nd trimester	Cases in 2nd trimester	<0.001**
Controls in 3rd trimester	Cases in 3rd trimester	<0.001**
Controls in 2nd trimester	Controls in 3rd trimester	<0.001**
Cases in 2nd trimester	Cases in 3rd trimester	<0.001**

**Highly significant

3rd trimesters and cases of both 2nd and 3rd trimesters (p<0.05) (table-IV).

DISCUSSION

Numerous studies have been conducted in the past to determine serum Hcy in both mild and severe form of preeclampsia but none compared serum Hcy levels in last two trimesters of normal pregnancies and preeclamptic primigravidas in Pakistan[13]. However, serum Hcy levels in second and third trimester of normal pregnancy and preeclampsia in primigravidas were not only determined but also compared in this study. In second trimester, serum Hcy levels were significantly increased in preeclamptics as compared to controls. A study concluded significant association between preeclampsia and eclampsia and maternal serum Hcy levels. A significant association between severity of preeclampsia and serum Hcy level was also studied[14]. While, in a longitudinal study conducted by Anna *et al*., there was no statistically significant difference was noted in Hcy levels of normal pregnancy and preeclampsia in early second trimester. The significant difference was only observed while studying Hcy between controls and preeclamptics at the time of delivery[15]. Lopez-Quesada *et al*. observed raised level of Hcy in controls of normal pregnancy in third trimester compared with controls of second trimester. Similarly, Hcy levels of controls and preeclamptic cases of third trimester were also studied and were significantly higher in cases than controls[16]. In our study, Hcy level (9.36 ± 0.25 µmol/L) in third trimester preeclamptics was significantly increased as compared to preeclamptics of second trimester (7.39 ± 0.38 µmol/L) (p<0.05). Another study concluded that plasma Hcy levels were significantly higher at the time of delivery (13.17 ± 3.89 µmol/L) but no statistically significant differences were observed in systolic and diastolic blood pressure[17]. Similarly, Hoque *et al*. found a positive association between hyperhomocysteinemia, preeclampsia, and eclampsia. Serum Hcy levels were measured and found higher in preeclamptics and eclamptics[18]. A positive association was also noted by another study in which mean serum level of Hcy was raised in preeclamptic cases than controls having normal pregnancy in third trimester[19]. Ingec *et al*. in 2005 has also proved positive association between plasma Hcy levels with the severity of preeclampsia. Mean Hcy levels of that study were significantly higher in cases of severe preeclampsia and eclampsia than controls and cases with mild preeclampsia. While, no statistically significant difference in Hcy levels between controls and mild pre-eclamptics was noted. This increase in Hcy concentration resulted due to severe form of preeclampsia[20]. In contrast, a study in 2004 suggested that Hcy levels were not due to presence of preeclampsia. Instead, females having raised Hcy tend to have a reduced risk of fetal loss, HELLP syndrome, and preeclampsia toxicosis[21]. Another study clearly correlated Hcy levels and hypertension[9]. In our study, a significant difference was observed in Hcy levels amongst preeclamptics and controls of 2nd and 3rd trimesters and also between controls of 2nd and 3rd trimesters and cases of both 2nd and 3rd trimesters. However, this study was carried out on a small group of pregnant females therefore caution needs to be exercised in generalizing the results.

CONCLUSION

There is a significant increase in serum Hcy levels in both second and third trimesters of pregnancies with preeclampsia as compared to controls.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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