ORIGINAL ARTICLE

Association of Serum Homocysteine Levels with Early and Late Onset Preeclampsia

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ABSTRACT

Objectives: To compare serum levels of homocysteine in woman having early onset and late onset pre-eclampsia.
Design of study: Descriptive cross sectional study.
Place and duration: MCH unit II, Pakistan Institute of Medical Sciences, Islamabad from 20th June 2016 to 20thMay 2017
Methodology: A total of one hundred and fifty patients between 20 to 40 years from 20-41 completed weeks of gestation with pre-eclampsia were included. Preeclampsia was further categorized into early and late depending on onset of P.E before or after 34 weeks. Patients using medications therapy involving anticonvulsant agents, 6-azauridine,anti-folic acids and tamoxifen, and having diseases like cancer or systemic major illness were excluded. Venous blood samples were withdrawn underaseptic technique. Serum homocysteinemeasurement was done by competitive chemo -luminescent enzyme immune assay method.
Results: Mean age was 30.45 ± 5.68 years. Majority of the patients i.e. 86 (57.33%) were between 31 to 40 years of age. Mean gestational age was 31.61 ± 5.09 weeks. Out of these 150 patients, 94 (64.42%) presented with early onset pre-eclampsia and 56 (35.58%) with late onset pre-eclampsia. Mean homocysteine levels in pregnant females with pre-eclampsia were 12.57 ± 3.11 µmol/L.(normal 8µmol/L)Comparison of mean homocysteine levels in pregnant females between early versus late onset pre-eclampsia did not show any statistical significance
Conclusion: Elevated homocysteine is associated with preeclampsia but without any difference between early and late onset P.E
Keywords: Pre-eclampsia, homocysteine levels, prognosis, early onset preeclampsia, Eclampsia, risk factors

INTRODUCTION

Pregnancy induced hypertension (PIH) presents in almost 3–10% of all pregnancies[1]. It is a major cause of maternal morbidity and mortality internationally because of its associated complications such as eclampsia, fetal growth retardation, DIC and placental abruption[1]. It is utmost important that at risk women should be identified earlier in pregnancy to allow proper fetomaternal surveillance. Preeclampsia has multiorgan pathology in whichmaternal vascular endothelium is the target of the inflammatory mediators arising from ischemic placenta and this widespread injury results in cerebral, renal and hepatic disorder[2].

Homocysteine is a sulfur-containing amino acid. It comes from the demethylation of methionine during nucleic acid methylation. Woman with homocysteinemia are at risk of diabetic microangiopathy, osteoporosis, cardiovascular disease and renal failure[3].Utero–placental oxidative stress plays acrucial role in placental related diseases like IUGR, abruption and pregnancy loss. It has been suggested that homocysteine has been involved in reactive oxygen species per oxidation. Normal serum homocysteine levels are between 4 and 15 micromoles/liter (µmol/L)

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Homocysteine levels more than 15 micromoles/liter are considered as hyperhomocysteinemia in non-pregnant woman while in pregnancy the upper limit is 8 micromoles/liter.A study quotes a mean homocysteine level in pre-eclampsia is 16.4µmol/L[1] while other states 11.42µmol/L[2] what so ever is value excessive homocysteine is associated withpre-eclampsia[1,2,3]. The folatesis involved in metabolism of homocysteine; its supplementation is known for preventing the neural tube defects andmiscarriage. Preeclampsia either late or early vary in terms of biomarkers, placental findings and feto maternal outcomes and it is difficult to find outthat these are qualitativedifferences representing unlike diseases, or quantitative differences within the same condition[4]. There are conflicting approaches to wards homocysteine testing and its value in the correlation of fetomaternal outcome in preeclampsia. The aim of the our study was to measure and compare serum homocysteine levels in woman presenting withearly onset and late onset preeclampsia to see its association with early or late placenta mediated pregnancy complications.

METHODOLOGY

This was a Descriptive cross sectional study conducted at MCH unit II, Pakistan Institute of Medical Sciences, Islamabad between 20th June 2016 and 20th May 2017. WHO sample size calculator was used to calculate sample

size taking confidence level = 95%, absolute precision = 0.10, Mean = 16.4, SD = 3.26. The sample size turned out to be 150. Non-probability purposive sampling was used in the selection of these patients.Approval of the study was taken from hospital ethical committee prior to start the study. Informed consent was obtained from each female and her partner. Patients between 20 to 40 years from 20-41 completed weeks of gestation with symptoms and signs suggestive of pre-eclampsia (Both early and late onset pre-eclampsia) supported by laboratory investigations and clinical diagnosis were included in the study.After history taking and examination, patients using medical therapyhaving 6-azauridine, anticonvulsant agents, antifolic acids , S-adenosyl-methionine, tamoxifen and xanthopterin; and woman having cancer, systemic major illnesswere excluded from the study. Under aseptic measures, venous blood samples were withdrawn when patient with pre-eclampsiawere admitted in HDU. The concentration of homocysteinewas checked by competitive chemo - luminescent enzyme immune assay method.Demographic profile like name, age, gestational age, parity, blood pressure, serum homocysteine levels and urinary albumin levels were entered in the Performa.

Data Analysis: The data analysis was done by using SPSS version 17. Mean±S.D was calculated for quantitative variables like age, gestational age, and parity and homocysteine levels. The homocysteine levels between early onset and late onset pre-eclampsia were compared by independent t test. Frequency and percentages were calculated for qualitative or categorical variable like early onset and late onset pre-eclampsia. Data was shown in the form of tables and graphs. $P<0.05$ was statistically significantly.Effect modifiers like age, gestational age and parity were controlled through stratification. Post-stratification independent 't' test was used to see the influence of these on outcome.

RESULTS

Out of these 150 patients, 94(62.67%) presented with early onset pre-eclampsia and 56 (37.33%) with late onset pre-eclampsia (Table I). Mean homocysteine levels in pregnant females with pre-eclampsia were 12.57±3.11µmol/L as shown in Table II. Comparison of mean homocysteine levels in pregnant females between early versus late onset pre-eclampsia does not show any statistical significance as delineated in Table III (p= .617)

Table-I: Distribution of patients according to onset of preeclampsia.

Onset of preeclampsia	n
Early	94(62.67%)
Late	56 (37.33%)
Total	150 (100%)

Table II: Mean homocysteine levels in pregnant females with pre-eclampsia.

	N	Minimum	Maximum	Mean	Std. Deviation
Homocysteine levels	150	8.0	17.0	12.5	3.1

Table III: Stratification of Mean homocysteine levels with respect to onset of preeclampsia,n=150

Onset of preeclampsia	Mean homocysteine levels		P-value
	Mean	SD	
Early	12.47	3.081	0.617
Late	12.73	3.176	

DISCUSSION

Homocysteine is an intermediate metabolite that has been implicated in thedisorders of the fetomaternal unit including preeclampsia, fetal growth restriction, placental abruption and recurrent pregnancy losses. Many studies have reported inconsistent associations between these complications and hyperhomocysteinemia.

Our study showed relationship of raised homocysteine levels with pregnancy mediated complication of preeclampsia like Vollset et al who found association of hyper-homocysteinemia with the preeclampsia, fetal growth restriction, prematurity, placental abruption and antepartum stillbirth; we observed the same in our study[5].

Many other former studies havereported risk of fetal growth restriction and small for gestational age babies with elevated homocysteine[6].

In contrary to this we found association of raised homocysteine levels with preeclampsia but observations of Bergen NE e tal. were against this relationship though like others they found association of raised homocysteine levels with small for gestational age babies that is also a known complication of uteroplacental insufficiency like preeclampsia[7]. Observations of Kharb S, in 2016 were in accordance to our study who reported elevated homocysteine and vitamin B12 deficiency during pregnancy as a risk factor for preeclampsia[8].

In many other studies[5], consistent with us, homocysteine level measurement have shown its increased concentrations in pregnancies complicated with preeclampsia but these results are different from Kahn SR who observed no association[9].

In a systematic review, Gaiday AN, showed that though, homocysteine levels range in uncomplicated pregnancies but sufficient data also indicated association of increased homocysteine levels inpregnancies complicated with PE, SGA andplacental abruption[10].

The results of Cheng PJ and Dodds L were like ours, stated an increased risk of preeclampsia related with higher homocysteine concentrations[11,12].

Scholten RR studied co-occurrence of prothrombotic and cardiovascular risk factors in preeclamptic women and observed that circulatory risk profile existed in two thirds of preeclamptic females and homocysteine levels were found raised in them[13]. These findings are consistent with our study and by Xu X who treated pregnant mice with homocysteine and found PE like symptoms i.e., raised blood pressure and proteinuria in treated mice[14]. Results of Chaudhry SH like ours, support an effect of elevated homocysteine in pregnancy on placenta related pregnancy complications[15,16].

CONCLUSION

Elevated homocysteine is associated with preeclampsia but without any difference between early and late onset P.E

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