ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 9, Issue – 6, November – 2024 , Page No. : 99 – 103

Study of Homocysteine, Vitamin B12 and Folic Acid Levels in Preeclampsia and Normotensive Pregnancy

[1]Dr Aparna Sasane, Associate Professor, Department of OBGY, SKNMC and GH, Dhyari, Pune

[2]Dr Vidya Gaikwad, Professor and HOU, Department of OBGY, Dr. D.Y. Patil Medical College and Hospital, Pimpri, Pune

[3]Dr Amol Sasane, Professor, Department of Radiology, SKNMC and GH, Dhyari, Pune

[4]Dr Hemant Deshpande, Professor and HOD, Department of OBGY, Dr. D.Y. Patil Medical College and Hospital, Pimpri, Pune

Corresponding Author: Dr Aparna Sasane, Associate Professor, Department of OBGY, SKNMC and GH, Dhyari, Pune

Citation this Article: Dr Aparna Sasane, Dr Vidya Gaikwad, Dr Amol Sasane, Dr Hemant Deshpande, "Study of Homocysteine, Vitamin B12 and Folic Acid Levels in Preeclampsia and Normotensive Pregnancy", IJMSIR - November - 2024, Vol – 9, Issue - 6, P. No. 99 – 103.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Introduction

Pregnancy induced hypertension may occur in about 5–8% of all pregnancies[1-6] In developing countries, hypertensive disorders are the second most common obstetrical cause of still births and early neonatal deaths, accounting for 23.6%. It is the third leading pregnancy related cause of maternal death, after hemorrhage and embolism (790 maternal deaths per1, 00,000 live births) [7,8].

Preeclampsia is one of the leading causes of maternal and perinatal morbidity and mortality[2,5] worldwide because of complications such as eclampsia, premature birth, fetal growth retardation or abruption placentae[9]. Despite a fairly high incidence, the underlying etiology of preeclampsia is still incomplete[10]. The treatment of preeclampsia is symptomatic till date, as the etiology of this condition has remained elusive for many centuries. Definitive treatment remains the delivery of fetus and placenta[10,11]. It is a progressive disorder; if the delivery is delayed it increases the risk of eclampsia and end organ damage threatening the lives of both mother and the baby.

The maternal serum homocysteine levels usually decrease with gestation. It may be due to a physiological response to the pregnancy, hemodilution from increased plasma volume or increased demand for methionine by both the mother and foetus[2,13,14].

High homocysteine levels might induce vascular damage through an endothelial dysfunction caused by oxidative stress in preeclampsia[1,16].

The present study was done to evaluate serum homocysteine, Vitamin B12 and Folic acid and their co relationship in patients of pre-eclampsia.

Materials and Method

A randomised controlled study was carried out at Department of Obstetrics and gynaecology, Dr. D.Y Patil Medical College, Hospital and Research Centre, Pimpri, Pune over a period of September 2013 to September 2016. Institutional Ethical Committee clearance was obtained. Informed and written consent of all patients

was taken. The study was conducted, on total 150 patients 75 pregnant women with pre-eclampsia and 75 normotensive pregnant women. Pre-eclampsia was diagnosed by blood pressure ≥ 140/90 mm of Hg on more than 2 occasions and persistent proteinuria > 30 mg/dl (>1 + dipstick) in random urine samples. Exclusion criteria were diabetes mellitus, chronic hypertension, renal or liver disease, H/o thromboembolism, smoking, anaemia, treatment with antifolates, anticonvulsant agents and theophylline.

Biochemical Analysis

Competitive chemiluminescent enzyme immunoassay was used to evaluate Serum homocysteine concentration. Normal values were between 3.7 and 16 umol/l. Measurement of serum Folic acid was done by boil competitive, liquid phase, ligand labeled, and protein binding chemiluminescent assay. Normal folate values were between 2.34 – 17.56 ng/ ml. Solid phase, competitive chemiluminescent assay method was used to measure serum vitamin B12 levels. Values between 187 and 883 pg/ml were considered normal.

Statistical Analysis

All the data was reported in terms of mean and standard deviation. Normal distribution 'Z' test was used for Statistical analysis. P-value < 0.05 was considered to be statistically significant and <0.001 highly significant.

Results

Table1: Demographics of Normal Pregnant and Preeclamptic women

Parameter	Normal Pregnancy (n=75)	Preeclampsia (n=75)
Age(yrs)	22.7±2.65	24.6 ±3.73
Gestational age (weeks)	37.62 ± 1.76	35.5±3.69
Systolic blood pressure (mm Hg)	112.4 ± 6.46	152 ±16.95
Diastolic blood pressure (mm Hg)	76.2± 5.56	104 ±12.06
Homocysteine	8.69 ± 1.43	24.7 ± 6.99
Folic acid	10.19 ± 1.53	9.32 ± 3.43
Vitamin B12	193 ± 3.97	175.8 ± 19.41

In our study it was found that preeclampsia is more common in primigravida (63%) than multigravida (37%). Also severe preeclampsia cases 54 cases (72%) were more than mild preeclampsia 21 cases (28%).

Table 2: Comparison between control and study group

Biochemical parameters	Preeclampsia	Control group	P value
Homocysteine	24.7±6.99	8.69±1.43	0.0000001
Vitamin B12	175.8±19.41	193±3.97	0.0000001
Folic acid	9.32±3.43	10.19±1.53	0.00004

The results from both the groups were compared. The values were presented in mean±SD.

P <0.05 significant, P<0.001 highly significant

In the study group of 75 diagnosed Pre-eclampsia cases, 62 cases (83%) had elevated serum homocysteine levels (>15umol/l) which is statistically highly significant (p<0.0000001) and 13 cases (17%) had serum homocysteine levels within normal range (<15 umol/l). In the control group all women had serum homocysteine levels within normal limits.

50 cases (67%) had decreased serum vitamin B12 levels (<187pg/ml) which is statistically highly significant (p<0.0000001) and 25 cases (33%) had serum vitamin B12 levels within normal range (<187pg/ml). In the control group all women had serum vitamin B12 levels within normal limits.

All the women in control as well as study group had serum folic acid levels within normal range (>2,34 ng/ml).

Discussion

Our finding suggests that levels of serum homocysteine and vitamin B12 are altered in preeclampsia patients than in age-matched normotensive pregnant control subjects [2].

In preeclampsia patients, SBP and DBP showed significant increase. Importance of these parameters has been recognized estimating cardiovascular disease risk factor due to their positive association with hypertension[1].

Homocysteine may prove to be the missing link in the etiology of pre-eclampsia[1].

In our study group, 21 cases were of mild preeclampsia, 54 cases had severe preeclampsia.

In the study group comprising of 75 diagnosed PE cases the mean serum homocysteine level was 24.7±6.99 umol/l which is statistically highly significant (p<0.0000001). The mean levels of homocysteine were almost increased by three times in preeclamptic patients than controls (24.7 vs.8.69 mol/l).

The mean serum homocysteine levels in patients with mild pre-eclampsia was 15.4 ± 4.23 umol/l and in patients with severe preeclampsia was 20.71 ± 4.20 umol/l, which when compared to normotensive pregnant women is elevated and is statistically highly significant (p<0.001). It shows strong association between increased blood pressure and homocysteine levels. This suggests that homocysteine levels are directly correlated with the severity of pre-eclampsia. Our study is supported by the study of Singh Urmila et al.[15], who found that the mean value in preeclamptic pregnant women was 13.6±3.5 umol/l in mild PE and 16.69±4.18 umol/l in severe PE group.

The mean serum homocysteine level in the control (normotensive pregnant women) group is 8.69±1.43umol/l. Our study is supported by various other studies viz., Singh Urmila et al.[15], Georgios Makedos et al.[16], Mujawar et al[3]. in which homocysteine level was in the range from 6.40 umol/l to 11.5±4 umol/l.

Levels of homocysteine are generally lowered during pregnancy[1]. The decrease in homocysteine levels which occurs in normal pregnancy do not occur in pre-eclampsia. Folic acid and vitamin B12 are required for the remethylation of homocysteine to methionine; vitamin B6 is required for the transsulfuration of homocysteine to cysteine[7]. In our study, the levels of vitamins B12 were significantly lowered in the preeclamptic as compared to control groups. It suggests that vitamin B12 deficiency could be the causative factor forhyperhomocysteinemia which correspondence with the study of Shahbazian N[2].

There was no significant difference in the folic acid levels in the preeclamptic and control groups, as patients were taking folic acid supplementation. Shahbazian N[2]did not found any differences in folic acid concentrations between preeclamptic and normal pregnant women. A limitation of our study is the lack of knowledge on the homocysteine status of the patients before the diagnosis of preeclampsia. We did not assess the vitamin B6, the cofactor in the transsulfuration pathway.

Hyperhomocysteinemia appears to be more common in patients with PE. The vascular endothelium in pregnant women may be more sensitive to homocysteine injury. Levels of homocysteine are generally lowered during pregnancy. However even a slight increase may lead to endothelial injury with subsequent activation of various factors that eventually results in preeclampsia.

Higher level of homocysteine increases the severity of pre-eclampsia. Levels of total homocysteine are positively correlated with systolic as well as diastolic blood pressure. The serum homocysteine was found to have negative and insignificant correlation with serum folic acid in preeclamptic patients. A good, negative and statistically significant correlation was found between serum homocysteine and vitamin B12 in preeclampsia.

Biochemical screening such as homocysteine, folic acid, vitamin B12 are of paramount importance in preeclampsia. The inverse relation between homocysteine and vitamin B12 indicates that severity of preeclampsia that can be contributed to CVD.

On the other hand, there is an absolute need for larger studies designed to answer the question as to whether hyperhomocysteinemia and vitamin B deficiency are associated with increased risk for CVD and whether therapy of these disorders might influence cardiovascular mortality.

References

1. Yadav, B.K., Maskey, S., Bhattarai, A. et al. Association of serum homocysteine with vitamin B12 and folate levels in women with pre-eclampsia in a tertiary health care center in Nepal. BMC Women's Health 24, 451 (2024). https://doi.org/10.1186/s12905-024-03284-9
2. Shahbazian N, Jafari RM, Haghnia S. The evaluation of serum homocysteine, folic acid, and vitamin B12 in patients complicated with preeclampsia. Electron Physician. 2016 Oct 25;8(10):3057-3061. doi: 10.19082/3057. PMID: 27957303; PMCID: PMC5133028.
3. Mujawar SA, Patil VW, Daver RG. Study of serum homocysteine, folic Acid and vitamin b(12) in patients with preeclampsia. Indian J Clin Biochem. 2011 Jul;26(3):257-60. doi: 10.1007/s12291-011-0109-3. Epub 2011 Jan 19. PMID: 22754189; PMCID: PMC3162959
4. Braekke K, Ueland PM, Harsem NK, Karlsen A,Blomhoff R, Staff AC. Homocysteine, cysteine, and related metabolites in maternal and fetal plasma in preeclampsia. Pediatr Res 2007; 62: 319-24.
5. Salam RA, Das JK, Ali A, Bhaumik S, Lassi ZS. Diagnosis and management of preeclampsia in community setting in low and middle-income countries. J Family Med Prim Care. 2015;4(4):501–6. doi:10.4103/2249-4863.174265.[PMC free article][PubMed][CrossRef][Google Scholar]
6. National high blood pressure education program working group report on high blood pressure in pregnancy. Am J Obstet Gynecol 1990 and revised 2000; 163:1691–1712.
7. Pregnancy, developed by the Task Force on Hypertension in (2013).*Hypertension in pregnancy*.
8. Zina Semenvskaya. 2010. “Preeclampsia”. Obstetrics-danilatos 02:34.
9. Shenoy V, Kanasaki K, Kalluri R. Pre-eclampsia: connecting angiogenic and metabolic pathways. TrendsEndocrinolMetab.2010;21(9):529-36.doi:10.1016/j.tem.2010.05.002. PMID:20646932.
10. Mohaupt M. Molecular aspects of preeclampsia. Mol Aspects Med 2007; 28: 169–91.
11. Shah MR. 2007. “Hypertensive Disorders in Pregnancy”.5.Etiopathogenesis of Pre-eclampsia:

current concept and the controversies.1st edition.P 39-47.

12. Brown MC, Best KE, Pearce MS, Waugh J, Robson SC, Bell R. Cardiovascular disease risk in women with pre-eclampsia: systematic review and meta-analysis. Eur J Epidemiol. 2013;28(1):1–19. doi: 10.1007/s10654-013-9762-6. [PubMed] [CrossRef] [Google Scholar]
13. Hague WM. Homocysteine and pregnancy. Best Pract Res Clin Obstet Gynaecol. 2003;17(3):459–69.doi:10.1053/S1521-6934)03)00009-1.
14. Walker MC, Smith GN, Perkins SL, Keely EJ, Garner PR.Changes in homocysteine levels during normal pregnancy. Am J Obstet Gynecol. 1999; 180:660–4.
15. Singh U, Gupta HP, Singh RK, Shukla M, Singh R,Mehrotra SS, et al. A study of changes in homocysteine levels during normal pregnancy and preeclampsia.J Indian Med Assoc 2008; 106: 503-5
16. Makedos G, Papanicolaou A, Hitoglou A,Kalogiannidis I, Makedos A, Vrazioti V, et al.Homocysteine, folic acid and B12 serum levels in pregnancy complicated with preeclampsia. Arch Gynecol Obstet 2007; 275: 121-4.