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International Journal of Clinical Biochemistry and Research

Journal homepage: <https://www.ijcbr.in/>

Original Research Article

Study of serum homocysteine, folic acid & vitamin B12 levels in preeclampsia patients of a tertiary care hospital

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ARTICLE INFO

Article history:

Received 28-01-2022

Accepted 15-02-2022

Available online 11-03-2022

Keywords:

Preeclampsia
Homocysteine
VitB12
Folic acid

ABSTRACT

Aims & Objectives: The present study is undertaken to assess the levels of serum homocysteine, folic acid and vitamin B12 and to find their correlation in pre-eclampsia patients.**Materials and Methods:** It was a cross-sectional, descriptive hospital-based study. The duration of the study was 12 months. The study was undertaken in Department of Biochemistry in collaboration with Department of Gynecology & Obstetrics of College of Medicine & JNM Hospital, Kalyani. Forty pre-eclamptic patients in the age group of 18–40 years were selected as cases & forty age & sex matched normotensive pregnant women were randomly selected as controls.**Results:** A total of 40 pre-eclampsia patients were studied majority (80%) of the participants belonging to Hindu community. Among the cases, serum homocysteine levels showed statistically significant increase ($P < 0.001$) whereas, folic acid and vitamin B12 levels showed significant decrease ($P < 0.001$). A negative and significant correlation was observed between serum homocysteine compared with vitamin B12.**Conclusion:** From the study it can be concluded that increased Homocysteine levels in pregnancy is a risk factor for development of preeclampsia.This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.For reprints contact: reprint@ipinnovative.com

1. Introduction

Preeclampsia is defined by appearance of hypertension & proteinuria after 20 weeks of gestation. It affects approximately 3–10% of all pregnancies.¹ It leads to maternal morbidity and mortality, because of several complications such as eclampsia, fetal growth retardation, and premature birth.² Though pregnancy induced hypertension (PIH) is regarded as a disease of unknown etiology, elevated homocysteine level has always been hypothesized as a key risk factor. Homocysteine is a sulphur containing amino acid, produced from the essential amino acid methionine in body. It undergoes transsulfuration reaction to produce cysteine or can be further remethylated

to produce methionine. The transsulfuration reaction requires vitamin B₆ as a coenzyme in presence of the enzyme cystathionine-β-synthase. Hyperhomocysteinemia is considered to be risk factor for cardiovascular diseases. An increase of 5 micromol/L of homocysteine in serum elevates the risk of coronary artery disease by as much as cholesterol increases of 20 mg/dl. Homocysteine interacts with lysyl residues of collagen and bind to fibrillin producing endothelial dysfunction. Conditions leading to high Homocysteine levels, such as low levels of folic acid and vitamin B12 can also increase the risk of vascular damage. It is therefore difficult to determine whether high homocysteine levels only or low concentrations of vitamin B12 and folic acid are atherogenic factors that leads to vascular damage leading to endothelial dysfunction.

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2. Materials and Methods

This study was carried out at Department of Biochemistry, in collaboration with Department of Gynecology & Obstetrics of College of Medicine & JNM Hospital, Kalyani. Patients who matched the inclusion criteria within the stipulated time duration (12 months) were included in the study population. At the end of 12 months, the number of patients was found to be 40.

40 pre-eclamptic patients in the age group of 18–40 years were enrolled in the study after obtaining detail medical history & taking informed consent. Parameters included Serum homocysteine, folic acid, and vitamin B12. 40 healthy normotensive pregnant subjects of identical age without any disease were randomly selected as controls.

2.1. Inclusion criteria

Patients with symptoms and signs suggestive of preeclampsia supported by laboratory investigations & with normal renal and liver function tests were included in the study.

2.2. Exclusion criteria

Either patient/caregiver who didn't provide written consent. Detailed drug history was obtained. Patients with history of medications such as, anticonvulsants, tamoxifen were excluded. Patients suffering from Cancer, Anemia, Systemic illness like diabetes & primary hypertension were excluded. History of major substance abuse & history of chronic inflammatory diseases were also excluded.

The Institutional Ethical Committee approved the study. Detailed informed consent was obtained from patients as well as control population.

2.2.1. Sample collection

2 ml of venous blood was drawn in clotted vial with aseptic precautions, following that it was centrifuged at 3000 rpm for 5 min.

Serum was aspirated for estimation of homocysteine, folic acid, vitamin B12. Hemolyzed & lipemic serum samples were discarded.

3. Materials and Methods

Serum Homocysteine, folic acid & Vitamin B12 concentration were measured by electrochemiluminescence immunoassay method using Cobas e411 analyzer.

Hyperhomocysteinemia was defined as a serum homocysteine concentration greater than 15 $\mu\text{mol/l}$.

3.1. Statistical analysis

The statistical analysis was done using SPSS 15.0 version. The continuous variables of demographic and biochemical parameters were presented as mean \pm S.D.

(standard deviation). Pearson correlation analysis was carried out to find the association (if any) of the confounding (independent) variables with biochemical parameters (dependent variables). The significance was considered with p values less than 0.05.

4. Results

Body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significant increased ($p < 0.05$) in cases as compared with control group (Table 1).

Table 1: Demographic parameters in cases & controls

Parameters	Control group (n=40)	Cases (n=40)	P value
Age	26.5 \pm 5.68	28.5 \pm 4.33	0.12
BMI	20.5 \pm 4.23	24.8 \pm 3.28	0.034*
SBP	118.2 \pm 5.08	148.4 \pm 6.76	0.01*
DBP	80.3 \pm 5.45	92.3 \pm 4.14	0.02*

Table 2: Serum homocysteine, folic acid & Vit B12 levels in cases & controls

Parameters	Control group (n=40)	Cases (n=40)	P value
Homocysteine ($\mu\text{mol/l}$)	9.58 \pm 3.67	17.1 \pm 4.12	0.008*
Folic acid (ng/ml)	11.92 \pm 3.02	8.93 \pm 3.44	0.04*
Vitamin B12 (pg/ml)	408 \pm 96.4	322.8 \pm 74.4	0.03*

As can be seen, significant increase (P value 0.008) were observed in serum homocysteine whereas, folic acid and vitamin B12 levels showed significant decrease ($P < 0.05$).

Table 3: Correlation between homocysteine levels with Folic acid & vitamin B12 levels in cases

Parameters	r value	p value
Folic acid	-0.23	0.34
Vitamin B12	-0.89	0.005*

A negative and statistically significant correlation was observed between serum homocysteine with vitamin B12. (Table 3).

5. Discussion

Our study shows that levels of serum homocysteine, folic acid and vitamin B12 are altered in preeclampsia patients than control population. It shows that there was significant hyperhomocysteinemia and deficiency of folic acid and vitamin B12 patients with preeclampsia.

Several factors may increase homocysteine levels in women with preeclampsia. Metabolism in the kidney is the major route by which homocysteine is cleared from

plasma and this route of elimination may be affected by preeclamptic changes in the kidney.

In our study, the levels of vitamins B12 and folic acid were significantly lowered in the preeclamptic as compared to control groups.

Hyperhomocysteinemia in such preeclamptic patients were found in our Study might be due to modulation in homocysteine metabolism, which corroborates with the work of Walker et al,³ Vollset et al⁴ & Hogg et al.⁵

Carmel R⁶ found that differences in folic acid concentrations are seen between preeclamptic and normal pregnant women.

Similarly, in a systematic review by Mignini et al,⁷ folic acid and vitamin B12 concentrations were lower in preeclamptic women when compared with those of normotensive women.

Homocysteine causes activation of Hageman's factor. This may lead to increased platelet adhesiveness and life-threatening intravascular thrombosis. Homocysteine also interacts with lysyl residues of collagen and bind to fibrillin, ultimately leading to endothelial dysfunction. In preeclampsia there is widespread endothelial dysfunction & vascular damage in body. Conditions leading to high Homocysteine levels, such as low levels of folic acid and vitamin B12 can also increase the risk of vascular damage.^{8–11} Hyperhomocysteinemia leads to coronary artery diseases. There is also some evidence to associate hyperhomocysteinemia with myocardial infarction. 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. Thereby providing adequate quantity of pyridoxine, Vit B12 & folic acid specially in pregnancy keeps homocysteine levels in blood to normal levels as their metabolism are interlinked. Maternal hyperhomocysteinemia thus leads to neural tube defects in foetus. Thereby high dose of folic acid is advised in pregnancy.

A good correlation between serum homocysteine and folic acid, and vitamin B12 levels observed in our study support this view.

6. Conclusion

From the above discussion we can assume that biochemical screening such as homocysteine, folic acid, vitamin B12 are of paramount importance in preeclampsia.

The inverse relation between homocysteine and folic acid, and vitamin B12 indicates that severity associated with metabolic disturbances in preeclampsia that can be contributed to CVD.

On the other hand, there is an absolute need for large 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.

Further studies should help define the role of genetic polymorphism in enzymes of homocysteine, folic acid, vitamin B12 metabolism and their role in preeclampsia.

7. Limitations

The number of patients included in this study was relatively low. A study with a significantly high number of cases can establish the facts far strongly.

8. Conflict of Interest

The authors declare that there is no conflict of interest in the study.

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Cite this article: Sur A, Koley S. Study of serum homocysteine, folic acid & vitamin B12 levels in preeclampsia patients of a tertiary care hospital. *Int J Clin Biochem Res* 2022;9(1):59-62.