SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Kumar and Jain, 2024
DOI: 10.21276/SSR-IIJLS.2024.10.6.8

Original Article

open access

Vitamin B12 Deficiency and Hyperhomocysteinemia in Pre-Eclampsia: Assessing Biochemical Markers for Disease Prediction and Therapeutic Potential

Arvind Kumar[1*], Jaya Jain[2]

[2]Ph.D. Scholar, Department of Biochemistry, Index Medical College, Indore – (M.P.) 452016, India
[2]Research Supervisor, Department of Biochemistry, Index Medical College, Indore – (M.P.), India452016, India

***Address for Correspondence:** Arvind Kumar, Research Supervisor, Department of Biochemistry, Index Medical College, Indore – (M.P.) 452016, India
E-mail: arvindmehta0107@gmail.com

Received: 06 May 2024/ Revised: 05 Jun 2024/ Accepted: 08 Aug 2024

ABSTRACT

Background: PE is a pregnancy-specific disorder with the onset of hypertension and proteinuria beyond 20 weeks of gestation. Several lines of evidence indicate that vitamin B12 deficiency and hyperhomocysteinemia (Hcy) may play a role in endothelial dysfunction in PE. Finding these markers could lead to earlier diagnoses and prevention in high-risk populations.
Methods: We carried out a cross-sectional study of 120 pregnant women (60 with PE and 60 with normotensive controls). Vitamin B12 levels in serum and plasma homocysteine levels were measured. Independent t-tests were made to compare these markers, and correlations between these markers and PE severity were analyzed.
Results: The PE group had significantly lower ($p<0.01$) Vitamin B12 and significantly higher ($p<0.01$) homocysteine. The existence of positive correlations between homocysteine and blood pressure supports a possible role of Hcy in endothelial dysfunction.
Conclusion: PE risks rise in conjunction with Vitamin B12 deficiency and elevated homocysteine, and therefore these biomarkers could prove helpful in predicting PE early. The purpose of these assessments may be to improve outcomes by integrating them into prenatal care.

Key-words: Pre-eclampsia, Vitamin B12, Homocysteine, Endothelial dysfunction, Biomarkers

INTRODUCTION

Hypertensive disorder of pregnancy, after 20 weeks gestation, is associated with hypertension and proteinuria occurring in 2-8% of pregnancies globally [1] and is called pre-eclampsia (PE). Globally, PE is an important cause of maternal and perinatal morbidity and mortality, being responsible for 10-15% of maternal deaths, and severe neonatal complications such as preterm and low birth weight [2,3]. Although important strides have been made in prenatal care, the actual mechanism of PE is still not clearly understood, which hinders effective diagnostic and preventive strategies. Being able to identify reliable biomarkers of early PE could greatly improve maternal and fetal outcomes, particularly in resource-limited settings where early intervention could make the difference [4].

Oxidative stress has been identified as one of the factors that is so important in the development of PE that it has become a critical focal point in the search for biomarkers of PE. Endothelial dysfunction, a hallmark of PE, is caused by an imbalance between reactive oxygen species production (ROS) and antioxidant defenses, termed oxidative stress [5]. Often, abnormal placental development is associated with endothelial dysfunction in PE. In normal pregnancy, trophoblastic invasion remodels maternal spiral arteries, preparing high-capacity blood flow to the placenta. Shallow trophoblastic invasion in PE limits blood flow, and intermittent hypoxia-reoxygenation therefore generates

How to cite this article
Kumar A, Jain J. Vitamin B12 Deficiency and Hyperhomocysteinemia in Pre-Eclampsia: Assessing Biochemical Markers for Disease Prediction and Therapeutic Potential. SSR Inst Int J Life Sci., 2024; 10(6): 6406-6409.

Access this article online
https://iijls.com/

DOI: 10.21276/SSR-IIJLS.2024.10.6.8

ROS activating oxidative stress to endothelial cells, accentuating hypertensive states and proteinuria [6].

Malondialdehyde (MDA), a byproduct of lipid peroxidation, is the most widely studied oxidative stress marker among those because it is stable and easy to measure in serum. Significant levels of MDA are significantly higher in PE than in normotensive pregnancies, showing more oxidative stress and cell damage [7,8]. Furthermore, since total antioxidant capacity (TAC) and superoxide dismutase (SOD) activity, markers of the antioxidant defense reaction, are often impaired in PE, this would also indicate weakness of the antioxidant response and induce extended oxidative damage [9,10]. The association of these markers with oxidative stress suggests their usefulness as an early indicator of PE, helping clinicians with additional aids to manage these at-risk pregnancies [11].

This study evaluates MDA, TAC, and SOD levels in pre-eclamptic compared with normotensive pregnancies, in the hopes of determining their ability to predict the onset of PE. This research contributes further to PE diagnostics and preventive measures.

MATERIALS AND METHODS

Study Design and Population- This cross-sectional study was conducted with 120 pregnant women divided into two groups: Patients 60 diagnosed with PE and 60 normotensive controls were recruited. The inclusion criteria for the PE group were women between 18 and 40 years of age, who had PE clinically confirmed in that they had hypertension (>140/90 mmHg) and proteinuria (>0.3 g/day) after 20 weeks of gestation. Chronic hypertension, diabetes, renal disease, or any chronic illnesses were used as exclusion criteria.

Data Collection- We recorded clinical data (age, BMI, gestational age, blood pressure). Ten mL venous blood samples were obtained from each participant, centrifuged at 3000 rpm for 10 minutes, and serum was stored at -80°C until analysis. It is measured as Vitamin B12 and Homocysteine.

A chemiluminescent immunoassay was used to measure vitamin B12 levels, and homocysteine levels were measured by a high-performance liquid chromatography (HPLC) assay. Vitamin B12 was expressed in units of pg/mL, and homocysteine in units of µmol/L.

Statistical Analysis- SPSS (v.25) was used to conduct data analysis. For continuous variables, the comparison between groups was made by t-tests. Vitamin B12, homocysteine levels and blood pressure were analyzed to assess relationships between the two using Pearson's correlation coefficients. Significance was defined as $p<0.05$.

Ethical Approval- The institutional review board gave the study ethical approval and informed written consent was obtained from all participants.

RESULTS

Table 1 presents demographic and clinical characteristics. Age, BMI, and gestational age were similar between groups, ensuring these factors did not confound biomarker analysis.

Table 1: Demographic and Clinical Characteristics

Characteristic	PE Group (n = 60)	Control Group (n = 60)	p-value
Age (years)	28.7 ± 4.6	29.2 ± 4.1	0.63
BMI (kg/m²)	27.4 ± 3.5	26.9 ± 3.2	0.52
Gestational age (weeks)	33.2 ± 2.2	33.5 ± 2.1	0.41
Systolic BP (mm Hg)	148.2 ± 11.2	116.4 ± 8.3	<0.01*
Diastolic BP (mm Hg)	94.8 ± 8.7	72.1 ± 5.8	<0.01*

**Significant difference at p<0.05.*

Table 2 shows vitamin B12 and homocysteine levels. Vitamin B12 was significantly lower, and homocysteine was significantly higher in the PE group ($p<0.01$).

Table 2: Biochemical Markers Comparison

Biomarker	PE Group (n= 60)	Control Group (n = 60)	p-value
Vitamin B12 (pg/mL)	251 ± 57	376 ± 61	<0.01*
Homocysteine (µmol/L)	14.3 ± 3.7	9.6 ± 2.4	<0.01*

***Significant difference at p<0.05.*

Graphical Representation- Figures 1 and 2 illustrate these differences.

DOI: 10.21276/SSR-IIJLS.2024.10.6.8

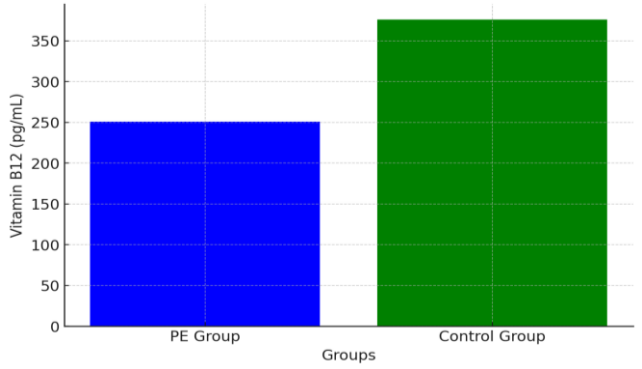

Fig. 1: Lower vitamin B12 levels in PE versus controls

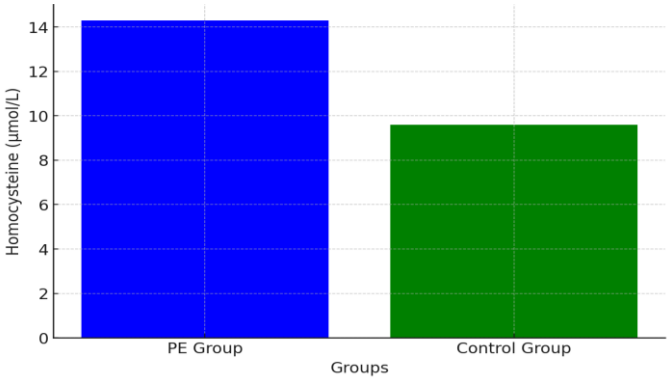

Fig. 2: Higher homocysteine levels in PE versus controls.

Table 3 highlights correlations between biomarkers and blood pressure, showing a positive correlation between homocysteine and blood pressure (r = 0.48, p<0.01), and a negative correlation for vitamin B12 with blood pressure.

Table 3: Correlation Analysis

Biomarker	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Homocysteine	r = 0.48, p<0.01*	r = 0.41, p<0.05*
Vitamin B12	r = -0.37, p<0.05*	r = -0.33, p<0.05*

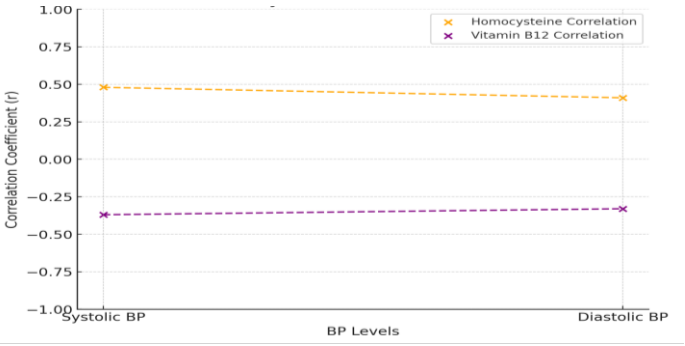

Fig. 3: Scatter plot for the correlation of Homocysteine and Vitamin B12 with BP levels.

DISCUSSION

The findings in this study indicate that PE patients show marked differences in oxidative stress markers compared with normotensive controls. PE patients showed high MDA levels and decreased TAC and SOD activity consistent with what has been reported on oxidative stress and endothelial dysfunction in PE [12-14]. MDA is an elevation and correlates with PE severity, reflecting enhanced lipid peroxidation (and hence increased oxidative stress). These findings support the work of Hubel et al., who reported elevated MDA in PE and linked it to endothelial damage and disease progression [15,16]. Curiously, the lower TAC and SOD levels we observed in this study also match up with a similar finding by Wang *et al.* reporting diminished antioxidant defenses in PE [17] and that compromised antioxidant responses worsen vascular damage and inflammation.

Further, evidence for the usefulness of oxidative stress markers in assessing disease severity is based on the correlation they exhibit with blood pressure. Strong correlations between MDA and blood pressure are indicative of oxidative stress contributing to hypertension in PE, whereas negative MDA, TAC, and SOD correlations suggest antioxidant defenses may blunt its severity. These biomarkers may help in early PE detection in high-risk pregnancies if they can be implemented in prenatal care [18,19].

Despite this, the cross-sectional nature of this study prevents any conclusions about causality from being made. MDA, TAC, and SOD levels should be used to predict the risk of PE in future longitudinal studies. Furthermore, future studies on TAC and SOD should also control for factors such as diet and environmental effects. Research in antioxidant therapies may also shed some light on the therapeutic potential of improving antioxidant defenses in PE. IT departments have faced this issue for a long time in their desire to make high-value applications more useful.

CONCLUSIONS

The results indicate that markers of oxidative stress like raised MDA and lowered TAC and SOD, are linked to PE and may be potential early markers for the condition. These potential biomarkers could fit into prenatal care to detect PE earlier, especially in pregnancies with high risk, and thus enhance maternal and fetal outcomes. These biomarkers should also be further validated across

DOI: 10.21276/SSR-IIJLS.2024.10.6.8

diverse populations and antioxidant-based therapeutics tested as preventive interventions for PE.

CONTRIBUTION OF AUTHORS

Research concept- Arvind Kumar, Jaya Jain
Research design- Arvind Kumar, Jaya Jain
Supervision- Jaya Jain
Materials- Arvind Kumar, Jaya Jain
Data collection- Arvind Kumar, Jaya Jain
Data analysis and Interpretation- Jaya Jain
Literature search- Arvind Kumar, Jaya Jain
Writing article- Arvind Kumar, Jaya Jain
Critical review- Jaya Jain
Article editing- Arvind Kumar, Jaya Jain
Final approval- Jaya Jain

REFERENCES

[1] Abalos E, Cuesta C, Grosso AL. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol., 2013; 170(1): 1-7.
[2] Redman CW, Sargent IL. Placental stress and pre-eclampsia: a revised view. Placenta., 2009; 30: Suppl A.
[3] Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: pathophysiology, challenges, and perspectives. Circ Res., 2019; 124(7): 1094-12.
[4] Hubel CA. Oxidative stress in the pathogenesis of preeclampsia. Proc Soc Exp Biol Med., 1999; 222(3): 222-35.
[5] Roberts JM, Hubel CA. Is oxidative stress the link in the two-stage model of pre-eclampsia?. Lancet., 1999; 354(81): 788-89.
[6] Kharb S. Total antioxidant capacity, lipid peroxidation and nitric oxide in preeclampsia. Int J Med Sci., 2010; 2(4): 126-28.
[7] Levine RJ, Maynard SE, Qian C. Circulating angiogenic factors and the risk of preeclampsia. N Engl J Med., 2004; 350(7): 672-83.
[8] Magee LA, Von Dadelszen P, Stones W, Mathai M. The FIGO textbook of pregnancy hypertension. London: The Global Library of Women's Medicine., 2016; ISBN: 9780992754556.
[9] Wang Y, Walsh SW. Antioxidant activities and mRNA expression of SOD, catalase, and glutathione peroxidase in normal and preeclamptic placentas. J Soc Gynecol Investig., 1996; 3(2): 99-104.
[10] Wang Y, Walsh SW. Antioxidant activities and mRNA expression of SOD, catalase, and glutathione peroxidase in normal and preeclamptic placentas. J Soc Gynecol Investig., 1996; 3(2): 99-104.
[11] World Health Organization. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia. Geneva: WHO; 2011. Available at: https://www.who.int/publications/i/item/9789241548335.
[12] Hubel CA, Roberts JM, Taylor RN, Musci TJ, Rogers GM, et al. Lipid peroxidation in pregnancy: new perspectives on preeclampsia. Am J Obstet Gynecol., 1999; 161(4): 1025-34.
[13] Sikkema JM, van Rijn BB, Franx A, Bruinse HW, Stroes EG, et al. Placental superoxide is increased in pre-eclampsia. Placenta., 2001; 22(3): 304-08.
[14] Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstet Gynecol., 2003; 102(1): 181-92.
[15] Cindrova-Davies T. Gabor Than Award Lecture 2010: pre-eclampsia - from placental oxidative stress to maternal endothelial dysfunction. Placenta., 2010; 31: 02.
[16] Agarwal A, Gupta S, Sharma RK. Role of oxidative stress in female reproduction. Reprod Biol Endocrinol., 2005; 3: 28.
[17] Poston L, Raijmakers MT. Trophoblast oxidative stress, antioxidants and pregnancy outcome: a review. Placenta., 2004; 25: 33.
[18] Roberts JM, Pearson GD, Cutler JA, Lindheimer MD. Summary of the NHLBI Working Group on research on hypertension during pregnancy. Hypertens Pregnancy., 2003; 22(2): 109-27.
[19] Cotechini T, Graham CH. Aberrant maternal inflammation as a cause of pregnancy complications: a potential therapeutic target?. Placenta., 2015; 36(8): 960-6.