

A Study on Pathophysiology, Diagnostic and Treatment Procedures for Preeclampsia Syndrome

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Abstract

Preeclampsia falls under a top priority pursued by the World Health Organisation. Despite several decades of extensive research into its aetiology, this disease has remained unknown. It seems that more than one pathophysiological factor contributes to increased blood pressure. With regard to the importance of preeclampsia, researchers have attempted to examine the hypotheses concerning the pathophysiology of the disease so as to obtain a broad approach to causes, possible treatments and early diagnosis. This study is based on the literature review relying on a total of 61 papers retrieved from several information banks and academic search engines, including, PubMed, Proquest, Elsevier and Scopus. These papers were selected through a number of designs such as cross-sectional, cohort, clinical trial and systematic review. Furthermore, the Persian papers were selected from databases such as Iranmedex and Medlib, as well as article search, on local web-based scientific journals. The investigation revealed that zinc plays a key role in prevention from preeclampsia. On the other hand, preeclampsia can be diagnosed, and potential risks can be evaluated based on measurements made during periods sooner than the third trimester. Moreover, preeclampsia can be treated by prescribing vitamin supplements and modification of diet. Furthermore, the additional supply of calcium has been useful in the treatment of preeclampsia in some areas, while it might be ineffective in some others. Finally, it can be argued that higher beta-human chorionic gonadotropin can indicate the severity of the disease, but it is of little value in early diagnosis of the medical condition. Having examined the studies done so far, it was found out that there are numerous parameters for early diagnosis and treatment of preeclampsia, even though they are far from comprehensive. These methods seem to be responding differently in every region. Therefore, it is recommended that such parameters be evaluated in various regions so as to pinpoint their effects.

Key words: Nitrite, preeclampsia, preeclampsia parameters, zinc

INTRODUCTION

The complications of pregnancy and childbirth every year lead to a great number of deaths in woman with gestational hypertension or preeclampsia.^[1] One of the issues concerning pregnant women and obstetricians is the incidence of preeclampsia. As a common disorder affecting 5–8% of pregnancies with complication, preeclampsia costs 5000 lives annually in women around the world.^[2] This syndrome is the second leading cause of maternal mortality worldwide right after vaginal bleeding.^[3,4] In developed countries, up to 25% of all prenatal deaths occur due to high blood pressure.^[5]

Preeclampsia is recognised as one of the major factors contributing to preterm delivery, intrauterine growth retardation, early placental abruption, prenatal asphyxia and

maternal mortality worldwide.^[6–8] This condition is observed in women experiencing their first pregnancy.^[5] The classic clinical protests entail blood pressure >140.90 after the 20th week of pregnancy (no previous history of hypertension), together with more than 300 mg of protein excretion in a 24-h urinary. Preeclampsia falls under a top priority pursued by the World Health Organisation. Despite several decades of extensive research into its aetiology, this disease has remained

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unknown. It seems that more than one pathophysiological factor contributes to increased blood pressure.^[6]

Preeclampsia is clinically obvious when the pathophysiology of the condition is approaching its final stages. Hence, it is crucial to examine the indicators assisting early diagnosis, which in turn brings about early treatment.^[2] Finally, with regard to the importance of preeclampsia, researchers attempted to review the literature revolving around preeclampsia, evaluated the hypotheses concerning various pathologies of the condition and obtained a broad insight into the causes, treatments and early diagnosis.

Since the detection of prenatal and maternal care can reduce the risk of premature birth^[9] or newborns at risk, therefore, this paper intends to examine several parameters such as nitrate, nitrite, malondialdehyde (MDA), ceruloplasmin, Vitamin C, calcium and beta-human chorionic gonadotropin (β HCG) as well as their role in early diagnosis and treatment for preeclampsia.

METHODOLOGY

This study is based on the literature review relying on several information banks and academic search engines such as PubMed, Proquest, Elsevier, Scopus and keywords, including, embryo, mother, birth weight and haematocrit. The articles were selected with a number of designs such as cross-sectional, cohort, clinical trial and systematic review. The Persian papers were selected from databases such as Iranmedex and Medlib, as well as article search, on local web-based scientific journals.

The time span for including the articles covered 1985 until 2012. Having run a preliminary search, a total of 35 articles were found and evaluated separately. At the end, 21 articles met the inclusion criterion, which was relevance to the research subject. The results of each article were carefully examined and elaborated based on the conclusions below.

A few instances of the articles applied in this study [Table 1]:

Table 1: Reviewed studies in this survey

Author	Research year	Remarks
Chang YJ, Lee WK, Kim HG	2007	Oxidative stress in rat model of preeclampsia and clinical correlates
Teran E, Chedraui P, Vivero S, Villena F, Duchicela F, Nacevilla L	2009	Plasma and placental nitric oxide levels in women with and without preeclampsia living at different altitudes
Rostami M, Jarafi M	2010	Evaluation of plasma level of nitrite, nitrate and MDA in preeclampsia
Necip I, Navin I, Mehmet S	2002	The changes of trace elements, MDA levels and superoxide dismutase activities in pregnancy with or without preeclampsia
Azizeh Ghaseminejad, Nasrin Khodadadi, Kermatar A. Nouri Jalyani, Mamak Jalilani, Elham Hashemian	2008	Relationship between serum level of ceruloplasmin and preeclampsia Journal of Medical Sciences School, Tehran University of Medical Sciences
MDA: Malondialdehyde		

Evaluation of serum level of zinc in preeclampsia

Zinc plays an important role during organogenesis and foetal growth.^[10,11] In most studies, the results showed that there was a significant relationship between low serum zinc level and preeclampsia. In their study in 2005, Rezavand *et al.* found out that the mean of zinc serum level in the preeclampsia group was 76.55 μ g/cc while it was 99.65 μ g/cc in healthy pregnant women. In fact, the comparison of the two groups indicated that subjects with preeclampsia had significantly lower zinc serum level ($P < 0.0001$).^[12] The study by Moghadam-Banaem *et al.* showed that reduced levels of zinc can contribute in affecting preeclampsia.^[13] Mokhlesi *et al.* study showed that reducing the daily intake of antioxidant nutrients (such as zinc) can contribute to the occurrence of preeclampsia.^[14] According to the results of these studies can be used to prevent pregnancy complications such as preeclampsia to understand and perhaps Prescribing mothers with zinc supplements might be beneficial. Finally, it is vital to conduct further studies on the prescription of zinc and how it affects the patients.

Evaluation of plasma level of nitrite, nitrate and malondialdehyde in preeclampsia

One of the most popular hypotheses about the aetiology of preeclampsia involves poor endothelial performance as a result of membrane lipid peroxidation.^[15] There are numerous factors contributing to physiological mechanisms of placental angiogenesis and regulation of vascular contraction that may in turn play an important role in the pathogenesis of abnormal placenta. One of the factors is nitric oxide.^[16]

One of the most important factors contributing to poor performance of endothelial cells is excessive levels of lipid peroxidase.^[17,18] The heightened MDA concentration may be due to increased production of oxygen free radicals caused by excessive oxidative damage in the patients. These reactive oxygen species can oxidise important biomolecules including membrane lipids. Lipid peroxides and free radicals may contribute to the pathogenesis of preeclampsia.^[19]

The results from the majority of relevant studies demonstrated the tremendous effect of nitrite, nitrate and MDA. In their study, Rostami *et al.* (2009) revealed that serum levels of nitrite, nitrate and MDA in the preeclampsia group were 6.12, 8.23 and 7.9 micromoles/L, respectively, while they were 7.8, 4.16 and 3.6 micromoles/L, respectively, in the control group, which indicated a statistically significant correlation between these substances and preeclampsia. In studies done by Pasaoglu *et al.*, Krishna Mohan and Venkataramana, Tug *et al.* and Adiga *et al.*, similar results were obtained, that is, plasma level of MDA in eclamptic patients was higher than that in the control group.^[20-23] Considering the increased level of these substances in preeclampsia, they might be useful as auxiliary tests in the diagnosis of preeclampsia or even the disease assessment of severity. On the other hand, the measurement of these substances before the third trimester may also facilitate the diagnosis or assess the risk of preeclampsia, preventive measures and treatment.

Evaluation of serum level of ceruloplasmin in preeclampsia

In a study done by Ghaseminejad *et al.* in Tehran (2009), the results indicated that mean of serum ceruloplasmin in women with severe and mild preeclampsia was significantly higher than that of the control group ($P < 0.001$). Moreover, the mean of serum ceruloplasmin in severe preeclampsia was higher than that in mild preeclampsia, while it was higher in early preeclampsia than in late preeclampsia ($P < 0.01$).^[24]

According to the study by Engin-Ustun *et al.*, ceruloplasmin in preeclampsia tends to rise in norm tension pregnant subjects. Such increase is greater in server preeclampsia than in the mild type, while it tends to be higher in the preterm type than in the late.^[4] The results obtained by Aksoy and Khetsurian also indicated that cerium ceruloplasmin rises in preeclampsia.^[25,26]

Given the facts mentioned above, it is recommended that women facing a high risk of preeclampsia have the serum level of certain chemical factors such as ceruloplasmin measured in order to prognosis the incidence of preeclampsia prior to emergence if medical symptoms, which would ultimately prevent prenatal maternal mortality and morbidity.

Furthermore, using antioxidants such as Vitamin C or E can postpone the course of preeclampsia.

Evaluation of plasma level of Vitamin C in preeclampsia

The vascular endothelial damage plays an important role in the pathophysiology of preeclampsia.^[27] Studies show that free radicals are present in the lipid peroxidation leading to damage in the endothelial cells.^[28] Antioxidants such as Vitamin C can hinder free radicals and their complicating outcomes.^[29]

In a study done by Dehghan *et al.*, the results indicated that mean of plasma level of Vitamin C in preeclampsia subjects was significantly lower than healthy pregnant women.

The more severe preeclampsia, the lower the serum Vitamin C,^[30] which is consistent with results obtained by Kharab.^[31] Finally, the measurement of Vitamin C can help diagnose preeclampsia and its severity, while the condition can be treated through prescribing vitamin supplements and a modified diet.

Evaluation of serum beta-human chorionic gonadotropin level in preeclampsia

The trophoblast dysfunction is an aetiology expressed in preeclampsia. Since β HCG is the serum reflecting the trophoblast activity, its measurement can be a reflection of varied secretory response in preeclampsia placenta, raising the possibility that such measurement can be helpful in the diagnosis of preeclampsia. In a study done by Akbari *et al.*, it was found out that β HCG was higher in the severe preeclampsia group as compared to the normal group and the mild preeclampsia, indicating no statistically significant difference. However, there was no significant relationship between the norm tension group and the mild preeclampsia group despite the β HCG level being higher in the mild group as compared to the norm tension.^[32] Other studies yielded similar

results.^[33,34] Finally, it can be argued that increased β HCG can indicate the disease severity, but proves little value in early diagnosis of the condition.

Evaluation of serum level of calcium in preeclampsia

Changes in calcium metabolism, as well as its deficiency, have been proposed as a hypothetical factor contributing to the pathophysiology of preeclampsia.^[35] It has been demonstrated that low levels of calcium can lead to vascular smooth muscle contraction and higher vascular resistance.^[36] There are controversial results obtained by studies on the role of calcium in preeclampsia. In their studies, Rudsari, Power and Richards observed no relationship between calcium and preeclampsia.^[35] But In studies done by Kosch and Seely results showed that there was a link between the loss of calcium and preeclampsia.^[36,37]

Furthermore, the studies by Nirumanesh, Kulier and Villar revealed that supplementary calcium diet leads to lower risk of preeclampsia.^[38,39] Having evaluated various relevant studies, it can be understood that different regions yielded non-identical results in examination of calcium for preeclamptic subjects, which is probably due to ethnic differences, nutrition and geographical conditions, etc. Therefore, it can be stated that the additional supply of calcium has been useful in the treatment of preeclampsia in some areas examined separately, while it might be ineffective in some others.

CONCLUSIONS

Having examined the studies done so far, it was found out that there are numerous parameters for early diagnosis and treatment of preeclampsia, even though they are far from comprehensive. These methods seem to be responding differently in every region. Therefore, it is recommended that such parameters be evaluated in various regions so as to pinpoint their effects.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Bath PM, Butterworth RJ. Platelet size: Measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis* 1996;7:157-61.
2. Cuningham FG, Levano KJ, Bloom SL, Hauch JC, Gilstrap LC, Wenstrom KD. *Williams Obstetrics*. 22nd ed. New York: McGraw Hill 2005. p. 762-8.
3. Lewis G, Drife J, Botting B. Why Mother Die, Report on Confidential Enquiries in to Maternal Deaths in the United Kingdom 1994-96. Department of Health, Welsh Office Scottish Office. Department of Health and Department of Health and Social Services. London: Stationery Office; 1983.
4. Engin-Ustün Y, Ustün Y, Kamaci M, Sekeroğlu R. Maternal serum ceruloplasmin in preeclampsia. *Int J Gynaecol Obstet*. 2005;89:51-2.
5. Granger JP, Alexander BT, Bennett WA, Khalil RA. Pathophysiology of pregnancy-induced hypertension. *Am J Hypertens* 2001;14 (6 Pt 2):178S-85S.

6. Wagner LK. Diagnosis and management of preeclampsia. *Am Fam Physician* 2004;70:2317-24.
7. Rukmini MS, Kowsalya R, Pai B, Das P, Perriera J, Nandini M, *et al.* Plasma adenosine deaminase activity and antioxidant status in preeclampsia compared to healthy pregnant and nonpregnant women. *Biomedical Research* 2009;20:15-20.
8. Larijani B, Marsoosi V, Moradi A, Hashemipour S. Assessment of Thyroid hormone changes in women with preeclampsia. *Iranian Journal of Endocrinology and Metabolism* 2001;3:106-1.
9. Namakin K, Sharifzadeh G, Malekizadeh A. To identify the risk factors in prematurity birth in Birjand, Iran: A case-control study. *IRJE* 2011;7:1-5.
10. Osendarp SJ, van Raaij JM, Arifeen SE, Wahed M, Baqui AH, Fuchs GJ. A randomized, placebo-controlled trial of the effect of zinc supplementation during pregnancy on pregnancy outcome in Bangladeshi urban poor. *Am J Clin Nutr* 2000;71:114-9.
11. King JC. Determinants of maternal zinc status during pregnancy. *Am J Clin Nutr* 2000;71 5 Suppl: 1334S-43S.
12. Rezavand N, Kiani A, Rezaie M. Study of serum zinc level in pregnant women with preeclampsia and comparison with normal pregnant women in Moatazedi Hospital, Kermanshah (2004 2005). *Urmia Med J* 2008;19:199 203.
13. Moghadam-Banaem L, Mokhlesi S, Mohebi S. Relationship between serum zinc level in early second trimester of pregnancy and preeclampsia. *Daneshvar Med J* 2013;20:47-54.
14. Mokhlesi S, Mohebi S, Moghadam-Banaem L. The survey of the daily intake rate of antioxidants' nutrients and their relation to preeclampsia among pregnant women from Tehran in 2012. *J Health Syst Res* 2014;10:618-27.
15. Ozan H, İlçöl Y, Kimya Y, Cengiz C, Ediz B. Plasma anti-oxidant status and lipid profile in non-gravida women with a history of pre-eclampsia. *J Obstet Gynaecol Res* 2002;28:274-9.
16. Teran E, Chedraui P, Vivero S, Villena F, Duchicela F, Nacevilla L. Plasma and placental nitric oxide levels in women with and without pre-eclampsia living at different altitudes. *Int J Gynaecol Obstet* 2009;104:140-2.
17. Lorentzen B, Henriksen T. Plasma lipids and vascular dysfunction in preeclampsia. *Semin Reprod Endocrinol* 1998;16:33-9.
18. Maseki M, Nishigaki I, Hagihara M, Tomoda Y, Yagi K. Lipid peroxide levels and lipids content of serum lipoprotein fractions of pregnant subjects with or without pre-eclampsia. *Clin Chim Acta* 1981;115:155-61.
19. Rostami M, Jorfi M. Evaluation of Serum nitrite, nitrate and malondialdehyde concentrations in preeclampsia. *J Reprod Infertil* 2010;11:105-12.
20. Adiga U, D'souza V, Kamath A, Mangalore N. Antioxidant activity and lipid peroxidation in preeclampsia. *J Chin Med Assoc* 2007;70:435-8.
21. Tug N, Celik H, Cikim G, Ozcelik O, Ayar A. The correlation between plasma homocysteine and malondialdehyde levels in preeclampsia. *Neuro Endocrinol Lett* 2003;24:445-8.
22. Krishna Mohan S, Venkataramana G. Status of lipid peroxidation, glutathione, ascorbic acid, vitamin E and antioxidant enzymes in patients with pregnancy – induced hypertension. *Indian J Physiol Pharmacol* 2007;51:284-8.
23. Pasaoglu H, Bukan N, Bulduk G, Celen S. Lipid peroxidation, nitrate and nitrite levels in eclamptic and intrauterine growth retarded pregnancies. *Turk J Med Sci* 2003;33:89-93.
24. Ghaseminejad A, Khodadai N, Jalilani KN, Shariat M, Hoshemian E. Correlation of serum ceruloplasmin with preeclampsia. *Tehran Univ Med J* 2009;66:761-6.
25. Power ML, Heaney RP, Kalkwarf HJ, Pitkin RM, Repke JT, Tsang RC, *et al.* The role of calcium in health and disease. *Am J Obstet Gynecol* 1999;181:1560-9.
26. Richards SR, Nelson DM, Zuspan FP. Calcium levels in normal and hypertensive pregnant patients. *Am J Obstet Gynecol* 1984;149:168-71.
27. Chapell LC, Seed PT, Briley AL, Kally FJ, Lee R, Hunt BJ, *et al.* Effect of anti-oxidants on the occurrence of preeclampsia in women at increased risk: A randomized trial. *Lancet* 1999;354:810-6.
28. Kyaw AA. Simple colorimetric method for ascorbic acid determination in blood plasma. *Clin Chim Acta* 1978;86:153-7.
29. Sibai BM. Prevention of preeclampsia: A big disappointment. *Am J Obstet* 1998;179:1275-8.
30. Dehghan M, Rajaei Far B, Ehdavand F, Amani F. Plasma levels of vitamin C in preeclampsic and normotensive pregnant women. *J Ardabil Univ Med Sci* 2004;4:26-31.
31. Kharab S. Vitamin E and C in preeclampsia. *Eur J Obstet Gynecol Reprod Biol* 2000;93:37-9.
32. Akbari S, Janani F, Changavi F, Ayazi M, Ghafarzadeh M. Beta-human chorionic gonadotropin (βHCG) levels in pre-eclamptic and normotensive pregnant women. *Yafteh (Persian)* 2005;7:57-62.
33. Gurbuz A, Karcteke A, Mengülluoğlu M. Can serum HCG values be used in differential diagnosis pregnancy complicated by hypertension? *Obstet Gynecol Istanbul Turk* 2004;23:1-12.
34. Zhonghua FU, Chan K, Zhi Z. Clinical significans of B-HCG and HPL in serum of normal pregnancies and patients with pregnancy induced hypertension? *Obstet Gynecol* 2000;35:648-50.
35. Vahid-Roodsari F, Ayati S, Torabizadeh A, Ayatollahi H, Esmaeli, Shahabian M. Serum calcium and magnesium in preeclamptic and normal pregnancies: A comparative study. *J Reprod Infertil* 2008;9:256 62.
36. Kosch M, Hausberg M, Louwen F, Barenbrock M, Rahn KH, Kisters K. Alterations of plasma calcium and intracellular and membrane calcium in erythrocytes of patients with preeclampsia. *J Hum Hypertens* 2000;14:333-6.
37. Seely EW, Wood RJ, Brown EM, Graves SW. Lower serum ionized calcium and abnormal calciotropic hormone levels in preeclampsia. *J Clin Endocrinol Metab* 1992;74:1436-40.
38. Niromanesh S, Laghaei S, Mosavi-Jarrahi A. Supplementary calcium in prevention of preeclampsia. *Int J Gynecol Obstet* 2001;74:17-21.
39. Villar J, Belizan JM. Same nutrient, different hypotheses: Disparities in trials of calcium supplementation during pregnancy. *Am J Clin Nutr* 2000;71:1375s-9s.