Asian Journal of Medicine and Health

19(11): 47-54, 2021; Article no.AJMAH.77295
ISSN: 2456-8414

Study of Antioxidants Vitamin E and Ascorbic Acid level in Pre-eclampsia and Normotensive Pregnant Women Attending the Antenatal Department of a Rural Hospital in Imo State South East Nigeria

C. J. J. Nnamdi [a*], E. C. O. Izuchukwu [a], I. S. Nwaisaac [b], S. C. Okeke [c], F. U. Ukodei [a], E. C. Ahams [d], R. I. Uzoma [b], O. G Iwuagwu [e] and A. A. Ezinwa [a]

[a] Department of Chemical Pathology, Faculty of Basic Clinical Science, College of Health Sciences, Nnamdi Azikiwe University Awka, Nnewi Campus, Anambara State, Nigeria.
[b] Department of Physiology, Faculty of Basic Medical Science, Nnamdi Azikiwe University, Nigeria.
[c] Department of Medical Laboratory Science Faculty of Health Science and Technology Nnamdi Azikiwe University, Nnewi Campus Anambara State, Nigeria.
[d] Department of Medical, Laboratory Services, Imo State University, Teaching Hospital Orlu, Nigeria.
[e] Department of Accident and Emergency, Federal Medical Center Owerri, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2021/v19i1130400
Editor(s):
(1) Dr. P. Veera Muthumari, V.V.Vanniaperumal College for Women, India.
Reviewers:
(1) Abrar Ul Hassan, University of Gujrat, Pakistan.
(2) Gamal Saad Elhadidy, Food Technology Research institute, Egypt.
Complete Peer review History, details of the editor(s), Reviewers and additional Reviewers are available here: https://www.sdiarticle5.com/review-history/77295

Original Research Article

Received 25 September 2021
Accepted 01 December 2021
Published 04 December 2021

ABSTRACT

Background: Deficiencies of nutrition are common during pregnancy especially in developing countries. Pregnant women in developing countries have been reported to consume diets that are low in minerals and vitamins. Inadequate dietary intake during pregnancy might be a high risk not only for the mother but also for the fetus. Deficiencies of antioxidant vitamins have been implicated in various reproductive disorders like infertility, congenital anomalies, pre-eclampsia, placental abruption, premature rupture of membranes, still births and low birth weight.

**Corresponding author: E-mail: cj.nnamdi@unizik.edu.ng;*

Objective/Aim: This investigation was performed to compare the level of serum antioxidant vitamin E and Ascorbic Acid status in women with preeclampsia and normal pregnancy in Imo State. It was a randomized cross sectional study of 50 preeclampsia and 50 normotensive pregnant women attending the Dept. of Medicine and Antenatal clinic of specialist Hospital Umuguma, Owerri Imo State Nigeria. The study protocol was reviewed and the ethical committee and participants gave their consent. Data analysis was done using the statistical package for social sciences (SPSS) version 20.0. P-value of < 0.05 was considered to be statistically significant.
Results: The mean antioxidant vitamins E and C were significantly lower in the preeclampsia group (0.29±0.07 and 0.31±0.20mg/dl) against the control (0.64±0.16 and 0.89±0.27mg/dl) P<0.05 respectively.
Conclusion: The study showed significant decrease in the level of vitamin E and Ascorbic Acid suggesting the failure of compensatory antioxidant functions in preeclampsia women.

Keywords: Antioxidants; pre-eclampsia; vitamin E; ascorbic acid (vitamin C).

1. INTRODUCTION

Pre-eclampsia defined as the onset of proteinuric hypertension after mid-pregnancy that affects about 3-10% of pregnancies. It remains a major cause of maternal and fetal morbidity and mortality worldwide. It is a rapidly progressive condition characterized by the development of hypertension and proteinuria after 20th week of gestation, characterized by high blood pressure, platelet Aggregation, swelling of the lower extremities and protein in urine [1]. It is the third most common cause of maternal death worldwide [2,3]. Developing countries are more unfavorably affected as about 65% of increased maternal mortality is associated with pre-eclampsia, while in developed countries it has been suggested to contribute to a five-fold increase in perinatal mortality responsible for 15% of preterm births [4]. Despite remarkable progress in the understanding of the pathophysiology of preeclampsia in the last few decades, the etiology of this disorder remains unclear; a problem compounded by its heterogeneity [5]. Pregnant women in developing countries have been reported to consume diets that are low in minerals and vitamins, as of recent, this disease cannot be cured and it usually leads to preterm caesarean delivery. In Nigeria, preeclampsia and eclampsia contribute 10–20% of all maternal deaths [3,6].

This disease starts pre-clinically and characterized by faulty trophoblastic vascular remodeling of uterine arteries that caused by release of placental factor's into the maternal circulation. Leading to systemic inflammatory response and endothelial activation [7]. It is widely accepted that endothelial cell dysfunction resulting in vascular permeability plays an important role in the pathophysiology of preeclampsia [3,8]. In normal pregnancy, the process of implantation, proliferation, differentiation and trophoblastic invasion, produce Reactive Oxygen Species (ROS), however in preeclampsia, lipid peroxidation, which also yields reactive oxygen species (in the form of free oxygen radicals), is uncontrolled [7,9]. It has been suggested that pregnancy will progress eventually if adequate antioxidants exist to buffer reactive oxygen species.[8,10,11] Nutritional deficiencies are common during pregnancy and pregnant women in developing countries have been reported to consume diets that are low in minerals and vitamins [12,13]. An inadequate dietary intake before and during pregnancy might be a high risk not only for the mother but also for the fetus [14,15].

This study assessed the level of antioxidant vitamin C (Ascorbic Acid) and vitamin E in normotensive and pre-eclamptic pregnancies. Thus this study was conducted in a cross-sectional manner to evaluate, the level of antioxidant vitamins between pre-eclampsia patients and normotensive patients.

2. MATERIALS AND METHODS

2.1 Study Design

This investigation was a cross-sectional randomized study designed to investigate the levels of antioxidant vitamin E and vitamin C in pregnant women with pre-eclampsia.

2.2 Study Area

This study was carried out in Department of Chemical Pathology, Nnamdi Azikiwe University

Nnewi Campus, located within the South-Eastern part of Nigeria. It lies in the latitude 5'27° - 5'31°N and the longitude 6'55° - 7'03°E. The climate of the area is tropical with mean daily temperature of 29±50°C for most of the year. The annual rainfall is between 217 and 240cm with distinct wet and dry season.

2.3 Study Population

The study population involves pregnant women attending the Department of Medicine and Antenatal care of Specialist Hospital, Umuguma, Owerri, Imo State, Nigeria. Calculated sample size for each group (n) was 50 using the formula n = 2Z2PQ/d2 using 95% confidence interval with 0.05 precision. A prevalence of 1.7% of preeclampsia in Nnewi a neighbouring town to Owerri as reported by Mbachu et al. [16] was employed. A total of 100 pregnant women were therefore recruited into the study who fulfill the inclusion criteria (comprising 50 pre-eclampsia and 50 normotensive group) informed consent was obtained from each of the subjects after the study was explained to them.

2.4 Exclusion Criteria

These include lactating mother, smoking, diabetic and alcoholic individuals, women with acute and chronic illness or taking any other medications that could potentially affect level of antioxidant vitamins were also excluded.

2.5 Blood Sample Collection

5ml of blood was drawn from the cubital vein using a sterile needle and syringe into an appropriate tube. The samples in plain tubes were allowed to clot undisturbed and serum were separated by centrifugation for 10mins at 4,000rpm into plain tubes and stored at -20°C until time of analysis.

2.6 Biochemical/laboratory Analysis

All reagent used was of analytical grade (AR). Antioxidant vitamin C was determined by Tietz method [17]. Antioxidant vitamin E was determined by Quaife et al [18] method, Quality control was ensured in the analysis of the samples by the use of commercially prepared samples ensuring that the same sensitivity and specificity were maintained.

2.7 Statistical Analysis

Data collected was analyzed using the SPSS software for windows version 20.0. Proportions were compared with Pearson Chi-square for categorical variables while means were compared using students t-test. Data were presented using tables. Values were set at 95% confidence level, a P-value of 0.05 was considered to be significant.

3. RESULTS

3.1 Anthropometric Parameters

Table 1 shows the clinical data on the preeclamptic women and healthy controls. The mean Age, BMI and HBC, of all preeclampsia patients was not statistically significantly different from those of control subjects($p>0.05$). There was a statistical significance difference ($p<0.05$) between the Systolic and Diastolic Blood Pressures of the Test and the Control group. The mean maternal and gestational ages of the subjects and controls were similar. Subjects had different gravida distribution and had nearly equal proteinuria.

Table 1. Comparison of maternal anthropometric characteristics between preeclamptic and normotensive pregnant women

Parameters	Preeclampsia (n=50)	Control (n=50)	t-test	P-value
Age(yrs)	25.0±1.64	25.5±1.70	-1.497	P>0.05
Gestational age (week) at sampling	35.23±1.64	34.64±0.95	5.289	p>0.05
Gravida in (%)				
primi	34(52.4)	28(40)	_	_
multi	16(28)	22(35)	_	_
BMI(kg/m2)	25.45±1.66	25.94±1.77	-1.427	P>0.05
SBP(mmHg)	147.04±5.9	115.96±4.9	28.66	P<0.05
DBP(mmHg)	96.96±6.54	80.04±9.87	10.11	P<0.05
HBC(g/dl)	10.05±0.58	10.33±0.48	-2.63	P>0.05

Parameters	Preeclampsia (n=50)	Control (n=50)	t-test	P-value
Proteinuriaprimi	2+(34)	0	_	_
multi	3+(16)	0	_	_

BMI: Body mass index; HBC: Haemoglobin Concentration; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; Values are mean ± standard deviation, P<0.05, n= total number of patients

Table 2. Comparison of serum concentration of vitamin C, and E in preeclamptic and normotensive pregnant women

Parameter	Preeclampsia(n=50)	Control(n=50)	t-test	p-value
Vit C (mg/dl)	0.31±0.20	0.89±0.27	-12.21	p<0.05
Vit E (mg/dl)	0.29±0.07	0.64±0.16	-14.17	p<0.05

Values are mean ± standard deviation, p<0.05

3.2 Biochemical/Laboratory Parameters

Table 2 Shows the mean value of plasma non-enzymatic antioxidants concentration (vitamin C and vitamin E) were significantly lower (p<0.05) in preeclampsia groups in comparison to the control group.

4. DISCUSSION

The results obtained from this investigation showed mean Systolic blood pressure of 147.04±5.9mmHg and a Diastolic blood pressure of 96.96±6.54mmHg in preeclampsia patients in contrast to a Systolic blood pressure of 115.96±4.9mmHg and a Diastolic blood pressure of 80.04±9.87mmHg in control subjects. This confirms an earlier investigation by Gifford et al. who reported a Systolic blood pressure of 140mmHg and a Diastolic blood pressure of 90mmHg. The slight difference in Gifford et al [19]. results and the value obtained in this investigation may be due to racial differences. The implication of this is that pathogenesis and development of complication may be more sever in preeclampsia patients in our environment (Nigeria) compared to Caucasians.

Some Studies has suggested that women with greater body mass index (BMI) in pregnancy are more likely to become hypertensive than those with lower BMI [20], but in this present study the comparable body mass index (BMI) observed in the preeclampsia and the control subjects contradict their findings on the influence of the body mass index on the aetiology or severity of preeclampsia in pregnant women.

Vascular endothelial damage has been shown to play a role in the pathophysiologic mechanism of preeclampsia [19,20,21]. It has been suggested that free radical mediated lipid peroxidation may be involved in endothelial damage seen in preeclampsia [19,21,22]. Excess free radical disturbances are typically accompanied by increased utilization of antioxidants resulting in a decrease in their concentration.

Some reports documented an increase in plasma vitamin E levels in pre-eclampsia [23,24]. But others have found a decreased concentration [7]. Vitamins E (alpha-tocopherol) and C, have differences in the contribution they make to antioxidant potential, as vitamin E is the major lipid soluble chain-breaking antioxidant in cell-membranes while vitamin C is an important aqueous phase antioxidant. Antioxidants may act synergistically, for instance when vitamin C regenerates alpha-tocopherol from the tocopherol radical [25,26] This 'sacrificial' antioxidant acts more by sparing vitamin E than by recycling [25,10]. Thus, it might be important to evaluate the effectiveness of potential antioxidant defense systems in limiting scale.

Several studies [27,28,13] measured vitamin E in the form of γ-tocopherol in the first trimester in one study, in the second trimester in three studies, and in the third trimester in and found no significant difference, but results suggested that higher levels may be associated with a modest increase in risk of preeclampsia. Wang et al, [29] Determined vitamin E levels longitudinally throughout normal pregnancy and observed a progressive increase in vitamin E concentration which was most prominent between 24 and 32 weeks, while others have reported decreased vitamin E levels during preeclampsia and normal levels in normotensive pregnant women [23,30,31,32]. It appears that water soluble antioxidants nutrients (reduced vitamin C) may be initially consumed followed by lipid soluble antioxidants (alpha tocopherol). Also it has been reported that vitamin C regenerates vitamin E by

non-enzymatic mechanisms [26,27]. In addition, vitamin C and vitamin E have been demonstrated to inhibit superoxide anion production in the pig coronary artery suggesting that beneficial effects of antioxidants vitamins are related in part to alterations in vessels redox status [33]. Furthermore, vitamin C treatment improves endothelial nitric oxide action in patients with coronary artery disease [33,34]. The decrease in antioxidant nutrients levels observed in this study supports the concept that free radical mediated lipid peroxidation may be involved in the pathophysiologic mechanism of preeclampsia mediated through oxidative stress [35,36].

This imbalance between lipid peroxidation and antioxidant defenses in preeclampsia leads to endothelial dysfunction and free radical mediated endothelial cell injury. Some studies [37,38], observed impaired antioxidant activity in women with preeclampsia. Palan et al. [35] found significantly lower levels of β-carotene, lycopene and xanthin in the sera and placentas of preeclamptic women than in the sera of normotensive women. many studies, [39,40] Observed that the risk of preeclampsia decreased with increasing concentration of α-carotene, β-carotene, β-crytoxanthin, lutein and zeaxanthin and they noted a 50% decrease in the risk of preeclampsia in women whose β-carotene concentration was in the highest quartile compared with women whose concentration was in the lowest quartile.

In the present study, it was observed that there was a fall in vitamin C levels in preeclampsia patients (0.31±0.25mg/dl), as against the control (0.89±0.27mg/dl). The value of vitamin E was lower in preeclampsia subject (0.29±0.07mg/dl) as against the control (0.64±0.16mg/dl). The result was in accordance with those reported by several studies [23,30,31,32]. Deleterious effects of free radicals include initiation of lipid peroxidation, oxidative damage of biomolecules, and cellular dysfunction, which may initiate maternal vascular endothelial dysfunction and leukocyte activation [41]. Free radical chain oxidation and the interaction of various antioxidants are now attracting the attention of nutritionists [42]. The important role of vitamin C and vitamin E in pre-eclampsia, suggests that changes in its concentration may influence susceptibility of vascular endothelium to oxygen toxicity [43,16,44]. Hence, analyzing vitamin C and vitamin E concentration may provide a means of assessing the total capacity of the chain-breaking antioxidants to prevent lipid peroxidation due to preeclampsia.

5. CONCLUSION

This investigation demonstrated that the level of antioxidant vitamin C and vitamin E are significantly altered in pregnant women with preeclampsia. It also suggest significant increase in lipid membrane damage activities (lipid peroxidation), as evidence by decreased level of antioxidant capacity in preeclampsia women. These further buttress a possible link between oxidative stress and preeclampsia. We recommend Vitamin E and Ascorbic Acid supplementation may help reduce the risk of pregnancy complications involving oxidative stress also the need to evaluate the efficacy and safety of vitamin E supplementation in pregnancy.

CONSENT

As per international standard or university standard, Participants' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

SPONSORSHIP

None

REFERENCES

1. Sarsam DS, Shamden M, and Wazan R .Expectant Versus Aggressive Management in Severe Pre-eclamptic remove from Term. Sing. Med. Journal. 2008;49:688.
2. Chukwudebelu WO, Ozumba BC. Maternal mortality at University of Nigeria Teaching Hospital, Enugu: A ten-year survey. Trop J Obstet Gynecol. 1998;1:21–26.
3. Unigbe JA, Orhue AA, Orosonye AU. Maternal mortality at the University of

Benin Teaching, Hospital, Benin City. Trop J Obstet Gynecol. 1998;1:13–18.

4. Roberts JM, Lain KY. Recent insights into the pathogenesis of preeclampsia. Placenta. 2002,23(5):359–72.

   Avaialble:https://doi.org/10.1053/plac.2002.0819 PMID: 12061851.

5. Roberts JM, Bell MJ. If we know so much about preeclampsia, why haven't we cured the disease? J Reprod Immunol. 2013;99(1–2):1–9.

   DOI: 10.1016/j.jri.2013.05.003 PMID: 23890710.

6. Audu LR, Ekele BA. A ten-year review of maternal mortality in Sokoto, Northern Nigeria. West Afr J Med 2002;2(1): 74–76.

7. Hansson SR, Naav A, Erlandsson L. Oxidative stress in preeclampsia and the role of free fetalhemoglobin. Front Physiol. 2015;5:516–532.

   Available:https://doi.org/10.3389/fphys.2014.00516 PMID: 25628568

8. Schmölz L, Birringer M, Lorkowski S, Wallert M. Complexity of vitamin E metabolism. World journal of biological chemistry. 2016;7(1):14.

9. Mohd Mutalip SS, Ab-Rahim S, Rajikin MH. Vitamin E as an antioxidant in female reproductive health. Antioxidants. 2018;7(2):22.

10. Rumbold A, Ota E, Hori H, Miyazaki C, Crowther CA. Vitamin E supplementation in pregnancy. Cochrane Database of Systematic Reviews. 2015:(9).

11. Hubalek M, Buchner H, Mörtl MG, Schlembach D, Huppertz B, Firulovic B, Köhler W, Hafner E, Dieplinger B, Wildt L, Dieplinger H. The vitamin E-binding protein afamin increases in maternal serum during pregnancy. Clinica Chimica Acta. 2014;434:41.

12. 12. Begum R, Begum A, Bullough C.H, and Johansin. R.B Reducing Maternal Mortality from Pre-eclampsia Using Magnesium Sulphate, European Journal of Obstetrics and Gynecology. 2000:92: 222-223.

13. Adam B, Malataliogu E, Alvur M, and Talu C. Magnesium, Zinc and Iron Level in Pre-eclampsia. Journal of Maternal and Foetal Medicine. 2001:10:246-250.

14. Mahommed K, Williams M.A, Woelk G.B, Mudzamini S, Madzine S, King IB, and Banksin DD. Leucocytes Selenium, Zinc and Copper concentrations in Pre-eclampsia and Normotensive Pregnant Women. Biol. Trace Elem. Res. 2004:269(13):9397-400.

15. Hofmeyr GT, Duley L, Atallah A. Dietary Calcium Supplementation for Prevention of Pre-eclampsia and Related Problems: A Systematic Review and Commentary. British Journal of Obstetrics and Gynecology. 2007:114(8):933-43.

16. Mbachu I, Udigwe GO, Okafor CI, Umeonunihu OS, Ezeama C, Eleje GU. The pattern and obstetric outcome of hypertensive disorders of pregnancy in Nnewi, Nigeria. Niger J Med. 2013; 22(2):117–22 PMID: 23829122

17. Tiezt, W. Ascorbic acid; in fundamentals of clinical chemistry Sixth edition. W.B Saunders Company, Britain. 2012; 476-496.

18. Quaife M.L, Scrimshan N.S, and Lowry O.H. A micromenthod for assay of total tocopherols in blood serum. J. Biol. Chem. 1940;180:1229-1236.

19. Gifford RW, August PA, Cunningham G, Green LA, Lindheimer MD, McNellis D, Roberts JM, Sibai BM, Taler SJ. Report of the national high blood pressure, education program working group on high blood pressure in pregnancy. American Journal of Obstst. And Gynecology. 2000;183: 1-22.

20. Pipkin FB. Risk factors for preeclampsia. N. Engl. Journal Med. 2000;344:925-6.

21. Kharb S, Gulati N, Singh V, and Singh G.P. Lipid peroxidation and vitamin E levels in preeclampsia. Journal of Gynecology and Obstetrics Invest. 1998;46(4);238-40.

22. Gupta S, Sinha A. Potential markers of endometriosis: Latest update. Journal of Genital System & Disorders; 2018.

23. Chapell LC, Seed PT, Briley AL, Kelly FJ, Lee R, Hunt BJ, Parmar K, Bewley SJ, Shennan A.H, Steer P.J,and Poston L. Effect of antioxidants on the occurance of preeclampsia in women at increased risk: a randomized trial. Lancet. 1999;354: 810-6.

24. Kyaw AA. simple colorimetric method for ascorbic acid determination in blood,

plasma. Clinical Chemistry Acta. 2005;86;153-7.

25. Romero R. Intrauterine infection, premature birth and the Fetal Inflammatory Response Syndrome. J Nutr. 2003;133: 1668S–1673S.
26. Sinha A, Gupta S. The role of antioxidant supplementation in endometriosis therapy. J Gynecol Women's Health. 2017:3.
27. Vitale SG, Capriglione S, Peterlunger I, La Rosa VL, Vitagliano A, Noventa M, Valenti G, Sapia F, Angioli R, Lopez S, Sarpietro G. The role of oxidative stress and membrane transport systems during endometriosis: a fresh look at a busy corner. Oxidative medicine and cellular longevity; 2018.
28. East-Powell M, Reid R. Medical synopsis: Antioxidant supplementation may support reduction in pelvic pain in endometriosis. Advances in Integrative Medicine. 2019;6(4):181-2.
29. 31. Wang Y, Walsh S.W, Guo J, and Zhang J. The imbalance between thromboxane and prostacyclin in preeclampsia is associated with an imbalance between lipid peroxides and vitamin E in maternal blood. American Journal of Obstetrics and Gynecology. 1991;165:1695-700.
30. Madazli R, Benian A, Gumustas K, Uzun H, Ocak V, Aksu F. Lipid peroxidation and antioxidants in pre-eclampsia. Eur J Obstet Gynecol Reproduct Biol. 1999;85:205-208.
31. Mikhail M.S, Anyaegbunam A, Garfinkel D, Palan P.K, Basu J, Romney S.L. preeclampsia and antioxidant nutrients, decreased plasma levels of reduced ascorbic acid alpha-tocoherol and beta carotene in women with preeclampsia. American Journal of Obstetrics and Gynecology. 1994;3(5):345-45.
32. Pourmasumi S, Ghasemi N, Talebi AR, Mehrabani M, Sabeti P. The effect of vitamin E and selenium onsperm chromatin quality in couples with recurrent miscarriage. International Journal of Medical Laboratory. 2018;5(1):1-0.
33. Nunes G.L, Robinson K, Ralynych A, King, S.B, Sgoutas D.S, and Berk B.C. vitamin C and E inhibit oxygen ion production in pig coronary artery. Circulation. 1999;96: 3593-601.
34. Hashemi Z, Sharifi N, Khani B, Aghadavod E, Asemi Z. The effects of vitamin E supplementation on endometrial thickness, and geneexpression of vascular endothelial growth factor and inflammatory cytokines among women with implantation failure. The Journal of Maternal-Fetal & Neonatal Medicine. 2019;32(1):95-102.
35. Palan PR, Mikhail MS, Rommy SL. placental and serum levels of carotenoids in preeclampsia. Journal of Obstetrics and Gynecology. 2001;98(3):459-62.
36. Chen H, Qian N, Yan L, Jiang H. Role of serum vitamin A and E in pregnancy. Experimental and therapeutic medicine. 2018;16(6):5185-9.
37. Spracklen CN, Smith CJ, Saftlas AF, Robinson JG, Ryckman KK. Maternal hyperlipidemia and the risk of preeclampsia: a meta-analysis. Am J Epidemiol. 2014;180(4):346–58.

    DOI:10.1093/aje/kwu145PMID:249892392: 243476.

    DOI:10.1100/2012/243476PMID:22593668
38. Yanik FF, Amanvermerz R, Yanik A, Celik C, and Kokcu A. preeclampsia associated with increased lipid peroxidation and decreased serum vitamin E levels. International Journal of Obstetrics and Gynecology. 1999;123(4)45-7.
39. Williams M.A, Woelk G.B, King I.B, Jenkins, and Mahommed K. Plasma carotenoids, retinol, tocopherols and lipoproteins in preeclampsia and nornotensive pregnant Zimbabwean women. American Journal of Hypertension. 2003;16(8):665-72.
40. Wei SQ, Julien P, Luo ZC, Audibert F, Fraser W. Maternal plasma beta-carotene, ICAM and VCAM levels in normal and preeclamptic pregnancies. Am J Epidemiol. 2012;175(Suppl 11):S79.
41. Raijmakers MT, Dechend R, Poston L. Oxidative stress and preeclampsia: rationale for antioxidant clinical trials. Hypertension 2004;44:374-380.
42. Kharb S. Vitamins E & C in pre-eclampsia. Eur J Obstet Gynecol Reproduct Biol. 2001, 1: 195-197
43. Agarwal A, Gupta S, Sharma RK. Role of oxidative stress in female reproduction. Reprod Biolo Endocrinol. 2005;3:28.

44. Schiff E, Friedman SA, Stampfer M, Kao L,Barrett PH, Sibai BM. Dietary consumption and plasma concentrations of vitamin E in pregnancies Complicated by pre-eclampsia. Am J Obstet Gynecol. 1996;175:1024-1028.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/77295