

# The Effects of Multi Vitamins Supplementation in the Prevention of Preeclampsia

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## Abstract

**Introduction:** Preeclampsia is a multifactorial pregnancy-specific disorder which is symbolized by the development of hypertension and proteinuria after 20 weeks of gestation. With the greatest morbidity and mortality, preeclampsia affects 5% to 7% of all pregnant women.

**Material And Method:** 390 subjects were included in the study and were grouped.

**Results:** Mean maternal age of cases in years was observed as 26.68±4.2, mean gestational age in weeks was 36.2. Systolic and diastolic BP in mmHg was 159.4 and 104.8 respectively. Mean weight was observed as 72.6 Kg and Height was 158.4 cm. There was statically significant correlation observed between vitamins in Group I and Group II, but Vitamin E and Vit B 12 does not show any significant correlation between them. No Stastical significance were found in the vitamins level in Group III and Group II. Statistically significant difference was observed between group I and Group III, for vitamin B12, vitamin D, vitamin C and vitamin A. No statistical significance difference was observed in vitamin E levels.

**Conclusion:** The intended intervention of Vitamins has a protective effect against recurrent preeclampsia. Vitamins supplementation therapy in pregnancy could help in reducing the incidence of gestational hypertension/preeclampsia.

**Keywords:** Pre-eclampsia, eclampsia, Vit B12, VitA, Vit C, Vit D and Vit E.

## Introduction

Eclampsia is a serious disorder affecting women during pregnancy. Early symptoms are known as pre-

eclampsia, which further develop to eclampsia and can land up in complications during pregnancy. Thus, eclampsia requires immediate medical treatment. Most cases are detected early in the pregnancy before developing eclampsia.<sup>[1]</sup>

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Preeclampsia is a multifactorial pregnancy-specific disorder which is symbolized by the development of hypertension and proteinuria after 20 weeks of gestation.<sup>[2]</sup> Hypertensive disorders is a common complication of pregnancy that put women and their foetuses at disproportionate risk for further complications, as well as life-long sequelae.<sup>[3]</sup>

PE is a very notable disease which complicates from 2% to 5% of pregnancies in Europe and America and can reach up to 10% of pregnancies in developing countries, mainly due to the lack of incompetence of emergency care. [3] According to the WHO its incidence is seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%). [4] PE is associated with an increased risk of placental abruption, preterm birth, foetal intrauterine growth restriction (IUGR), acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulation, and maternal death. [5]

With the greatest morbidity and mortality, preeclampsia affects 5% to 7% of all pregnant women but it is responsible for over 70 000 maternal deaths and 500 000 fetal deaths worldwide every year. [6]

### Preeclampsia progresses in 2 stages:

- A. Abnormal placentation early in the first trimester followed by
- B. Maternal syndrome in the sequentially second and third trimesters characterized by an excess of antiangiogenic factors. [7]

The end stage of pre-eclampsia is eclampsia which is defined by generalized seizures, with or without raised blood pressure and proteinuria, occurring during or after pregnancy with or without other identifiable cause. The cause is usually multifactorial including cerebral vasoconstriction, ischemia, vasogenic edema, or other pathology. In the first stage, abnormal placentation and deficient spiral artery remodeling leads to placental ischemia. Placental ischemia in turn influence on the clinical manifestations of preeclampsia, including the development of hypertension and proteinuria. Although eclampsia occurs mostly in women with severe pre-eclampsia, there is no convincing test for predicting its onset. [8-11]

**Aim:** Correlation of Vitamins levels before and after supplementation in pre-eclampsia

**Objective:** To determine serum vitamin A, C, D, E, B12 levels in pregnant women attending maternity clinic at AVBRH Wardha and SMHRC Nagpur.

## Material and Method

The present Study was carried out in the Department of Biochemistry and Dept. of OBGY at Datta Meghe Medical College, Shalinitai Meghe Hospital & Research Centre, Nagpur in collaboration with Jawaharlal Nehru Medical College and AVBRH (Datta Meghe Institute of Medical Sciences), Sawangi (Meghe) Wardha Maharashtra.

**Study Population:** 390 subjects were included in the study and were grouped as under.

**Group 1:** 90 pre-eclampsia diagnosed subjects without any supplementation.

**Group 2:** 90 pre-eclampsia diagnosed subjects with supplementation.

**Group 3:** 210 Normal pregnant women.

**Study Type:** Cross sectional interventional study

**Statistical Analysis:** All estimated results were expressed as mean±SD. Mean values will be assessed for significance by unpaired student -t test. A statistical analysis will be performed using the Statistical Package for the Social Science program (SPSS, 24.0). Frequencies and percentages will be used for the categorical measures. Probability values  $p < 0.05$  will be considered statistically significant.

## Observation and Results

**Table 1: Baseline Characteristics**

Variables	Cases (n=90)
Maternal Age (years)	26.68±4.2
Gestational Age (weeks)	36.2
Systolic BP(mmHg)	159.4
Diastolic BP (mmHg)	104.8
Weight(Kg)	72.6
Height (cm)	158.4

Table no. 1 shows that mean maternal age of cases in years was observed as 26.68±4.2, mean gestational age in weeks was 36.2. Systolic and diastolic BP in mmHg was 159.4 and 104.8 respectively. Mean weight was observed as 72.6 Kg and Height was 158.4 cm.

**Table 2: Levels of Vitamins before and After Supplementation.**

Vitamins	Group I Mean±SD (n=90)	Group II Mean±SD (n=90)	Group III Mean±SD (n=210)
Vitamin B12	149±40.09	195.67±104.34	264.4±269.57
Vitamin D	10.73±3.46	12.43±4.43	14.67±17.82
Vitamin A	0.325±0.143	0.63±1.10	0.92±2.144
Vitamin E	5.44±7.725	5.7±7.80	6.49±9.13
Vitamin C	0.38±0.172	0.53±0.531	0.77±1.63

**Table no 2 shows** the mean values in Group I, Group II and Group III of Vit B 12, Vit D, Vit A, Vit E and Vit C were (149±40.09, 195.67±104.34, 264.4±269.57), (10.73±3.46, 12.43±4.43, 14.67±17.82), (0.325±0.143, 0.63±1.10, 0.92±2.144), (5.44±7.725, 5.7±7.80, 6.49±9.13), (0.38±0.172, 0.53±0.531, 0.77±1.63) respectively.

**Table 3: Correlation of Vitamins levels in pre-eclamptic and after supplementation.**

Vitamins	Group I	Group II	t-value	p-value
Vitamin B12	149±40.09	195.67±104.34	-3.93	0.50
Vitamin D	10.73±3.46	12.43±4.43	-2.84	0.0024
Vitamin A	0.325±0.143	0.63±1.10	-2.73	0.0034
Vitamin E	5.44±7.725	5.7±7.80	-0.27	0.390
Vitamin C	0.38±0.172	0.53±0.531	-2.81	0.002

P value <0.05 Significant

**Table no 3 shows** there was statically significant correlation observed between vitamins in Group I and Group II, but Vitamin E and Vit B 12 does not show any significant correlation between them.

**Table 4: Correlation of Vitamins levels in normal with supplementation.**

Vitamins	Group III	Group II	t-value	p-value
Vitamin B12	264.4±269.57	195.67±104.34	-2.343	0.0198
Vitamin D	14.67±17.82	12.43±4.43	-1.176	0.2405
Vitamin A	0.92±2.144	0.63±1.10	-1.780	0.0716
Vitamin E	6.49±9.13	5.7±7.80	-0.716	0.4744
Vitamin C	0.77±1.63	0.53±0.531	-1.365	0.1733

P value <0.05 Significant

**Table no 4 shows** no Stastical significance were found in the vitamins level in Group III and Group II.

**Table 5: Correlation of Vitamins levels inpre-eclamptic with normal.**

Vitamins	Group I	Group III	t-value	p-value
Vitamin B12	149±40.09	264.4±269.57	-4.038	0.001
Vitamin D	10.73±3.46	14.67±17.82	-2.079	0.0385
Vitamin A	0.325±0.143	0.92±2.144	-2.628	0.0090
Vitamin E	5.44±7.725	6.49±9.13	-0.954	0.3408
Vitamin C	0.38±0.172	0.77±1.63	-2.262	0.0244

P value <0.05 Significant

**Above table no 5** shows that statistically significant difference was observed between group I and Group III, for vitamin B12, vitamin D, vitamin C and vitamin A. No statistical significance difference was observed in vitamin E levels.

## Discussion

The prevalence of PE has been reported to be 5-7% of all pregnancies, mainly due to the lack of or inadequacy of emergency care. PE is associated with an increased risk of placental abruption, preterm birth, foetal intrauterine growth restriction (IUGR), acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulation, and maternal death. PE is a leading cause of maternal mortality it affects both mother's and foetuses health during pregnancy.<sup>[12-16]</sup> Epidemiological research suggested that preeclampsia has a multifaceted etiology that includes an immunogenetic component<sup>[17]</sup> Established risk factors include nulliparity, family history of preeclampsia–eclampsia, and preeclampsia in a previous pregnancy, obesity, increased insulin resistance, hyperlipidemia, multiple gestation, molar pregnancy. Protective factors include a prior completed pregnancy and a terminated pregnancy for women conceiving again with the same partner<sup>[18-21]</sup>, therefore, PE prevention is highly crucial. 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 pre eclamptic changes in the kidney.<sup>[22]</sup> Similarly, in a systematic review by Mignini et al., folic acid and vitamin B12 concentrations were lower in pre eclamptic women when compared with those of normotensive women.<sup>[23]</sup> From early pregnancy placenta assumes a state of oxidative stress arising from increased placental mitochondrial activity and leads to the production of reactive oxygen species (ROS), mainly superoxide anion.<sup>[24,25]</sup> In preeclampsia, an increased level of oxidative stress is seen. The source had been allocated to the placenta, where free radical synthesis occurs, with maternal leukocytes and the maternal endothelium likely contributors.<sup>[26,27]</sup> The superoxide-producing enzyme NADPH oxidase, shown to be present in placental trophoblast. Women with early onset of preeclampsia have been found to have increased superoxide production compared with those with late-onset disease.<sup>21</sup> However, clinical trials of antioxidant therapy with vitamins C (1000 mg) and E (400 IU) have been dismayed and were associated with an increased

number of low-birth weight babies in the treatment-<sup>[28]</sup> So in this study we are trying to see the role of Vitamin in PE, as preeclampsia remains a challenge to diagnose. Therefore, the ability to provide an early diagnosis of PE is vital for health of both mother and fetus. A study conducted by **A. P. Mackay, C. J. Berg et. al**<sup>[6]</sup> studied that Mortality from preeclampsia and eclampsia increased with increasing maternal age. A study conducted by **Azami M, Azadi T, Farhang S et. al**<sup>[7]</sup> studied that the incidence of preeclampsia in group A was significantly lower than the control group ( $p=0.03$ ), while there was no significant difference between group B and controls ( $p=0.50$ ), as well as groups A and B ( $p=0.063$ ). The incidence of neonatal complications in the group A was significantly lower than the control group ( $p=0.01$ ), while there was no significant difference between group B and control ( $p=0.48$ ). The present study concluded that multiminerals and vitamin D during pregnancy can be a low-cost and affordable way to reduce the incidence of preeclampsia in women who are at high risk of preeclampsia. A study done by **Rudra P, Basak S, Patil D, Latoo MY**<sup>[8]</sup> concluded that out of 8,524 deliveries, 104 cases of pre-eclampsia were documented giving an overall prevalence of 1.2%. The prevalence in 2009, 2010, and 2011 was 0.7%, 1.2%, and 1.5%, respectively. Fifty-nine case notes were available for analysis (56.7% retrieval). The mean age of the patients was  $27 \pm 4.9$  and majority; 25 (42.4%) were in the age group 25-29 years. The mean parity was  $1.1 \pm 1.4$  and 26 (44.1%) were nulliparous. 11 (18.6%) had family history of hypertension, 2 (3.4%) had personal history of hypertension, and 2 (3.4%) had a personal history of preeclampsia. The slight increase in the prevalence rate over the years underscores the need for close surveillance. A study done in 2016 by **Hariharan N, Shoemaker A, Wagner S**<sup>[9]</sup> concluded that preeclampsia remains a complex disease process with multiple components intertwined in its development including angiogenic and endothelial dysfunction. A study done by **Mayrink J, Costa ML, Cecatti JG**<sup>[10]</sup> figured that preeclampsia is still one of the main causes of death and severe maternal morbidity. A case control study was carried out in the Neonatal Division, JNMCH, in 2018 by **Prasad D, Smita KS, Nisha S**<sup>[19]</sup> In the study 208 mothers were divided into two groups with newborns birth weight <2.5 kg (cases) and 2.5 kg or more (controls). Maternal vitamin D levels were estimated. Maternal vitamin D statuses of both groups were compared. Study done by **Rajmakers MT, Dechend R, Poston L**<sup>[20]</sup> concluded that Preeclampsia remains a frequent

and potentially dangerous complication of pregnancy. A study done by **Bastos Maia S, Rolland Souza AS et. al**<sup>[21]</sup> concluded that adequate levels of vitamin A during pregnancy are of critical importance for the health of pregnant women and their fetuses. Study done by **Mujawar SA, Patil VW, Daver RG**<sup>[22]</sup> evaluated the occurrence of association between homocysteine, folic acid and vitamin B<sub>12</sub> in patients with preeclampsia. A study conducted by **Mignini L, Latthe P et. al**<sup>[23]</sup> concluded that Homocysteine concentrations are slightly increased in normotensive pregnancies that later develop preeclampsia and are considerably increased once preeclampsia is established, because of a lack of consistency in data, dose-response relationship, and biologic plausibility, the observed association cannot be considered causal from the current literature.

### Conclusion

Our study findings suggest that levels of Vitamins are altered in Pre-eclampsia patients. Maternal vitamins deficiency can lead to serious complications. Supplementation with vitamin C and E may be helpful in reducing the risk of preeclampsia. The intended intervention of Vitamins has a protective effect against recurrent preeclampsia. Vitamins supplementation therapy in pregnancy could help in reducing the incidence of gestational hypertension/preeclampsia.

**Ethical Clearance:** Taken from institutional ethics committee.

**Source of Funding:** Self.

**Conflict of Interest:** Nil.

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