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Research Article

EFFECTS OF VITAMIN E IN HYPERTENSIVE DISORDER OF PREGNANCY AND ITS OUTCOMES

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ABSTRACT

Objective: To investigate the effects of vitamin E in Hypertensive Disorder of Pregnancy and the effects of vitamin E in Pregnancy Outcomes in Hypertensive Disorder of Pregnancy.

Study Design: Prospective Cohort Study

Materials and Method: A total of 1910 pregnant women visited to the OPD and admitted in the Obstetrics and Gynecology Department of the First Affiliated Hospital of Dali University in Yunnan Province from June 2017 to May 2018 fulfilling the inclusion criteria were included in our study group. All the pregnant women between the ages 23 to 35 years were included in the study and were divided into four groups: Normal pregnant group, gestational hypertension group, Pre-eclampsia group, and severe Pre-eclampsia group. Normal pregnant women were included in this group.

Statistical Method: This study was performed prospectively and collected data were statistically analyzed using SPSS software (version 20.0) using independent t-test, Pearson Chi-square test, and one-way ANOVA test. The P values considered significant at value $P<0.05$. The descriptive data were presented using frequency and percentage. Multivariate Logistic regression analysis was conducted to examine the effect of vitamin E in HDP and Pregnancy outcomes including PPH, HIE, Neonatal rescue and 1≤Apgar Score≤7.

Results: There was no statistically significant difference in the results of all studies on BMI, WOG in the third trimester, parity, and maternal age ($P>0.05$) There was no significant difference between the hypertensive group and control group during pregnancy in vitamin E level ($t=1.665$ $P=0.096$) ($P>0.05$).The difference between pre-eclampsia and severe pre-eclampsia group was statistically significant in vitamin E level ($t=27.692$ $P=0.000$) ($P<0.05$). When vitamin E was excess, there was no significant difference between the control group, the gestational HTN group, pre-eclampsia group and severe pre-eclampsia group ($X^2=0.164$, $P=0.983$) ($P>0.05$). When vitamin E was deficient, the difference between the control group and the hypertensive group during pregnancy was statistically significant ($X^2=20.580$, $P=0.00$) ($P<0.05$). When

vitamin E was deficient, there was no significant difference between the pre-eclampsia group and severe pre-eclampsia group (X^2=0.827, *P*=0.399) (*P*>0.05).In Gestational Hypertension group there is 8.3% occurrence of PPH, 8.3% newborn has HIE. In pre-eclampsia group, there is 10% occurrence of PPH, 5% newborn has HIE, 5% newborn needed neonatal rescue and 5% newborn has 1≤Apgar Score≤7. In severe pre-eclampsia groups there is 5.7% occurrence of PPH, 5.7% newborn has HIE, 5.7% newborn needed neonatal rescue and 2.9% newborn has 1≤Apgar Score≤7. (X^2=2.325, *P*=0.887) (*P*> 0.05) There was no significant difference in the incidence of 1≤Apgar Score≤7 and Neonatal rescue between the pre-eclampsia and the severe pre-eclampsia.

Conclusion: Vitamin E contents are related to the hypertensive disorder of pregnancy. Vitamin E deficiency is related to the occurrence of hypertensive disorders of pregnancy and has effects on maternal health and fetal outcomes.Serum levels of vitamin E detection during pregnancy can help in the prediction of hypertensive disorder of pregnancy; hence, it can help to reduce the risk of Pre-eclampsia.

Keywords: Vitamin E, Gestational Hypertension, Pre-eclampsia, Pregnancy outcome.

Effects of vitamin E in Hypertensive Disorder of Pregnancy and its Outcomes:

Background: Hypertensive Disorder of Pregnancy (HDP) is defined as high blood pressure ≥140/90 mmHg with that develops after 20 weeks in pregnancy and goes away after delivery. HDP is a common complication of pregnant women and one of the important causes of high maternal and infant mortality [1, 12, 13, 14]. Worldwide, the incidence rate of HDP is 4%-15%[15]. In China its 3.5% -9.8%[2]. HDP can lead to a serious condition called Pre-eclampsia, also referred to as Toxemia. Pre-eclampsia is a disorder of pregnancy characterized by Pregnancy Induced Hypertension (≥140 mmHg systolic blood pressure and ≥90 mmHg diastolic blood pressure)and new-onset proteinuria(≥300mg protein/d) occurring in the mid-half of pregnancy. Pre-eclampsia is a multi-organ disease and can affect the kidney, liver, brain and the blood clotting system [3,4].

HDP can be divided into Preeclampsia and severe Preeclampsia according to the severity of the disease. Severe Preeclampsia is the major cause of maternal and fetal morbidity and mortality [24]. The pathogenesis and etiology of HDP have not been fully elucidated so far but in recent years it has been found that nutritional deficiency and vitamin deficiency such as vitamin E may also be associated with HDP. This disease not only endangers the safety of pregnant women and fetuses but also has a harmful impact on the future health of mothers and children. People with Hypertensive disorder of pregnancy and their offspring have an increased risk of cardiovascular and cerebrovascular disease in the future [17]. So it is very important to understand the risk factors of its onset, to prevent and intervene as early as possible and to prevent the occurrence of adverse pregnancy outcomes.

Etiology, pathogenesis, and pathophysiology of pre-eclampsia: The etiology of preeclampsia is largely unknown [32], but several theories have been put forward and several studies suggest that the oxidative stress may be involved in the pathogenesis [9,10].The exact cause of pre-eclampsia, often referred to as a 'disease of theories', remains unknown, however, the placenta plays a major role in the pathophysiology of pre-eclampsia and it has, therefore, long been referred to as a placental condition. Generally accepted theories for

the etiology of Hypertensive Disorder of Pregnancy are "insufficient placental blood perfusion" and "excessive activation of inflammatory immunity" and mechanism of placental variation and insufficient placental oxygen supply. Although the placenta is necessary for pre-eclampsia, poor placentation is not the cause of preeclampsia, but rather important predisposing factors. Other pregnancies, such as those complicated by IUGR, preterm deliveries are also associated with abnormal placentation but do not develop pre-eclampsia. It has also been suggested that pre-eclampsia results from a mismatch between uteroplacental supply and fetal demands, which leads to its systemic inflammatory maternal (and fetal) manifestations [38,39]The most common maternal manifestation define pre-eclampsia clinically: hypertension and proteinuria. Other manifestations may be end-organ dysfunction and are non-specific. Pulmonary edema and stroke are leading causes of maternal death in pre-eclampsia[40,41]. Fetal manifestations may occur before, with, or in the absence of maternal manifestations [42] and consist of oligo-hydramnios, IUGR [43], abnormal umbilical artery Doppler resistance, an abnormal ductus venosus wave-form and/or stillbirth.

This paradox has led to the hypothesis that pre-eclampsia is a two-stage disorder, with reduced placental perfusion representing stage-one, while stage-two refers to the multisystemic disorder or maternal syndrome produced in response to reduced placental perfusion that is influenced by genetic or environmental maternal constitutional factors. Oxidative stress suggests the linkage between these two [23]. There is a hypothesis given which predicts that administration of antioxidants would decrease oxidative stress and modify stage- two [23].Endothelial activation appears to be central of the pathophysiological changes associated with pre-eclampsia [32], with circulating markers of endothelial activation increased in pre-eclampsia and in those women destined to pre-eclampsia.It has been proposed that an unknown factor excreted from the placenta is central of pre-eclampsia, such as placental debris, apoptotic, lipid peroxidation products or other reactive oxygen species, all of which are able to induce maternal oxidative stress directly or indirectly.

An abnormal healthy pregnancy is associated with a systemic inflammatory response. Such an inflammatory response can cause or be caused by endothelial dysfunction and oxidative stress.Thus there are increasing pieces of evidence that oxidative stress plays an important role in the pathogenesis of pre eclampsia[9,10], perhaps acting as the link in the two-stage model of pre-eclampsia.

Oxidative stress and antioxidant defenses: Oxidative stress is defined as an imbalance between oxidants and antioxidants in favor of oxidants, which potentially leads damage. It follows that there must be either an increase in oxidant or a reduction in antioxidants, for disturbances in this balance to occur [26]. Oxidative stress arises when the production of reactive oxygen species overwhelms the intrinsic antioxidant defenses. Reactive oxygen species play important roles as second messengers in many intracellular signaling cascades aimed at maintaining the cell in homeostasis with its immediate environment [36].Oxidants or reactive oxygen species (ROS) include free radicals, such as $0H^-$, O_2^- , and NO^- and also include the reactive molecules H_2O_2, the peroxynitrite anion ($ONOO^-$) and HOCl. Free radicals are defined as any molecular species capable of independent existence that contains an unpaired electron and their production occurs continuously in all

cells as part of normal cellular functions. Excess production of free radicals is thought to play the role in many diseases including pre-eclampsia. The process of uncontrolled lipid peroxidation leads to cellular dysfunction and damage as such oxidative stress. Oxidative stress is both a cause and a consequence of hypertension [37]. Hence, antioxidative stress is involved in the etiology of pre-eclampsia [27].

Antioxidant defenses system plays a key role in protecting against oxidative stress. This system includes the chain-breaking antioxidants such as vitamin E and the antioxidant enzymes. Chain-breaking antioxidants are small molecules that can either receive an electron from a radical or donate an electron to a radical to form stable by-products. Vitamin E, an important chain-breaking antioxidant scavenges radicals in membranes and lipoprotein particles and is central to the prevention of lipid peroxidation. Oxidative stress has been implicated in the pathophysiology of pre eclampsia[32]. The antioxidant activity is reduced in a woman with pre-eclampsia compared with women with normal pregnancy. The antioxidant activity begins to increase early in pregnancy8-12 weeks and gradually increase throughout gestation and at late gestational age 33-40 weeks and remains at this level until delivery within 24 hours of delivery, levels begin to decline. Insufficient Vitamin E may lead to complications such as Pre-eclampsia and SGA, Small for gestation age (baby being born small).

Lipid peroxidation in pregnancy: Lipid peroxides and oxygen radicals are highly reactive and very damaging compounds. In normal pregnancy lipid peroxides increase, but antioxidants also increase to offset their toxic actions. However, in the case of pre-eclampsia women, circulating levels of lipid peroxides are increased but net antioxidant activity is decreased as compared to normal pregnant women [34].

Classical risk factors for pre-eclampsia include: Maternal obstetric factors-the extremes of maternal age (women in their early teens and those over the age of 40), nulliparity, new male partner, multiple gestations, gestational hypertension, obesity, chronic hypertension, preexisting diabetes, and other less-common medical conditions, such as renal disease, systemic lupus erythematosus and antiphospholipid antibody syndrome. Despite this set of known risk factors, not all women with these risk factors develop the disorder, and not all the women presenting with pre-eclampsia have specific underlying risk factors [29].

The relationship between the antioxidant as vitamin E and the Pre-eclampsia: Vitamin E, as a potent antioxidant can inhibit lipid peroxidation and can prevent endothelial cell damage and protect blood vessels. It is an important intramembrane antioxidant and membrane stabilizer [35]. It is found in many foods including vegetable oils, cereals, meat, poultry, eggs, fruits, vegetables, and wheat germ oil. It is also available as supplements 400IU daily. The reference range of vitamin E in adults 5.5-17microg/ml, in children, it is 3-18.4 µ/ml. Vitamin E also plays an important role as free radicals during pregnancy. Pregnancy is the state in which there is a vigorous increase in the metabolism, which enhances the lipid peroxidation reaction resulting in the increase of free radicals. If not managed in the time, may lead to an increase in the risk of pregnancy-induced hypertension, placental aging and even in the adverse effect on the pregnancy outcomes [20]. The deficiency of vitamin E can cause accumulation of lipid peroxidation products, which, in turn, can cause vasoconstriction [33].

Vitamin E is a potent antioxidant. Oxidative stress has been proposed as a key factor involved in the development of pre-eclampsia. Lack of vitamin E lead to an imbalance between the oxidation system and antioxidant system.Supplementation with vitamin E during pregnancy may help to counteract oxidative stress and thereby prevent or delay the onset of pre-eclampsia.

Diagnosis: Diagnostic criteria of pre-eclampsia include new onset of elevated blood pressure and proteinuria after 20 weeks of gestation. Features such as elevation of BP above the baseline and edema are no longer the diagnostic criteria [7,8]. The diagnosis of pre-eclampsia is clinical. As defined by the American College of Obstetrics and Gynecology, the diagnosis requires blood pressure >140/90 mmHg on 2 occasions combined with urinary protein excretion > 300 mg/d. Edema, a classic feature of the disease, nowadays is no longer considered a diagnostic feature given its lack of sensitivity or specificity[34]. Laboratory tests, such as liver function tests, quantification of urinary protein, and serum creatinine may be helpful in characterizing the degree of end-organ damage but none is specific for pre eclampsia[35].

Common causes of maternal and fetal morbidity and mortality in pre-eclampsia: Include MOF, Intravascular hemolysis, cerebral hemorrhage, HELLP syndrome, etc.Premature birth and fetal distress may occur in the influence of intrauterine fetus. Other serious problem includes IUFD, IUGR, neonatal HIE, Poor Apgar Score.

Hypertensive Disorder of Pregnancy not only risk the health of mothers and infants and harm to the pregnant and fetus during pregnancy but also may bring potential risk to the future CVD of mother and infants. It is therefore of great significance to prevent the occurrence of PIH to reduce the incidence and to prevent and intervene in advance for the outcome of mother and children.

Abnormal levels of Vitamin E in Hypertensive Disorder of Pregnancy may also be related to the other complications are follows: Small for gestation age (SGA)-Several mechanisms have been proposed to describe how oxidative stress may lead to SGA. Oxidative stress may lead to placental infarction or placental calcification, resulting in suboptimal placental function and restricted fetal growth [11]. Oxidative stress may also contribute to the risk of SGA by provoking endothelial dysfunction, which is known to occur in isolated SGA, although to a lesser extent than has been demonstrated in pre-eclampsia. Spontaneous Abortion, M. SIMSEK and other studies found that the serum levels of vitamin E in women with habitual abortion were significantly lower than those in women without abortion [31].

Birth Defects-Lack of Vitamin E can cause abnormal development of eyes, heart, lungs, kidneys, bones and nervous system. Excessive vitamin E can lead to neural tubular, craniofacial and membranous heart diseases. Dutch studies have shown that vitamin E supplementation with food and drugs can lead to congenital heart disease in the fetus. The incidence increased by 9 times.

Gestational Diabetes Mellitus- vitamin E have anti- chlorination activity, especially vitamin E is a chain-breaking antagonist, which can effectively protect islet cells from oxidative damage. The serum levels of vitamin E in stable urine disease decreased significantly.

Several types of research and studies have shown that the serum vitamin E level during the smoking

period affects iron absorption, distribution, transport and is closely related to Iron Deficiency Anemia [31]. Smoking decreases tubal cilia numbers. Supplementation of Vitamin E may treat or least help to slow down the decrease in the number of cilia caused by smoking; therefore it could be therapeutically in the treatment of smoking-related tubal disease [10].

Premature Rupture of Membrane-When Premature Rupture of Membrane occurs, the production of reactive oxygen species (ROS), especially superoxide anions, in pregnant women increases, the consumption of large amounts of SOD,

Yunnan Province is located in the plateau, terrain area. Due to the influence of dietary habits, the lack of vitamin E is common during Pregnancy. Hence, it has become a high-risk group for Hypertensive Disorder of Pregnancy. Vitamin E deficient pregnant women are monitored throughout pregnancy to ensure that its level is maintained. It is, therefore, necessary to ensure that maternal complications during pregnancy are reduced and fetal development has adequate nutritional support at a reasonable level.

As vitamin E is a potent antioxidant, it plays an important role in antioxidation and free radical scavenging process. Pregnancy is the state in which the body metabolism increases vigorously which leads to an increase in lipid peroxidation reaction and also increase of free radicals. As a result, leads to placental aging, increase the risk of gestational hypertension and its various adverse effects.Therefore, maternal serum level during pregnancy is related to the incidence of Hypertensive Disorder of Pregnancy which has become the research of this paper.

So, if one method is used to predict the occurrence and development of Hypertensive Disorder of Pregnancy before the onset of hypertension and to reduce the risk factors of hypertension, the occurrence of perinatal maternal hypertension will be effectively reduced.To improve the survival rate of perinatal infants, this experiment was designed to measure the serum levels of pregnant women in the third-trimester pregnancy.

OBJECTIVES

The main purpose of this study was to investigate the effect of vitamin E in Hypertensive Disorder of Pregnancy.

Other objectives: To determine the effects of vitamin E in pregnancy outcomes in Hypertensive Disorder of Pregnancy.

MATERIALS AND METHODS

General situation: 1910 pregnant women admitted in Gynecology and Obstetrics Department of First Affiliated Hospital of Dali Hospital, Yunnan Province from January 2018 to May 2018was included in our study. The gestational age of the patient was between 32 to 38 weeks and their age was between 23 to 35 years.

Case selection: All the pregnant women of gestational age between 32 to 38 weeks and the age between 23 to 35 years were included in the study and were divided into four groups: Normal pregnant group,

Gestational hypertensive group, pre-eclampsia group, and severe pre-eclampsia group.Among them, there were 1000 cases in the control group (normal pregnancy), 300 cases in the Gestational hypertensive group 250 cases in the mild pre-eclampsia and 360 severe pre-eclampsia group.

Inclusion criteria: Pregnant women of age between 27 to 35 years, pregnant women of gestational age between 32to 38 weeks, no history of chronic hypertension, no previous history of Gestational Hypertension

Exclusion criteria: Pregnant women with Diabetes mellitus, Chronic HTN, Liver diseases Kidney, Thyroid and other endocrine diseases, Metabolic diseases, Twins or Multiple pregnancies, Smoker.

Control group: Normal pregnant women were included in this group.

Diagnostic criteria for Hypertensive Disorder of Pregnancy:

Gestational hypertension: BP ≥140/90 mmHg appears after 20 WOG and disappears till 12 weeks of delivery.

Pre-eclampsia: Systolic BP ≥140mmHg, Diastolic BP ≥90mmHg with proteinuria>0.3g/24hrs after 20 WOG or random protein (+).

Severe Preeclampsia: Continuous elevation of BP.Systolic BP ≥160mmHg, Diastolic BP ≥110mmHg with proteinuria>5.0g/24hrs after 20 WOG or random protein(+++) associated with other symptoms like persistent headache, visual impairment, systemic edema, thrombocytopenia, hypoproteinemia, damaged liver function, significant increase in transaminase, plasma alkaline phosphates, complicated with renal dysfunction , heart failure , cerebral hemorrhage or pulmonary edema.

Eclampsia: Pre-eclampsia complicated with convulsions and /or edema.

Diagnostic criteria for Vitamin E: According to the specification of the kits and the criteria adopted in most literature, and the standard reference of our hospital.Vitamin E levels were grouped according to:1) Normal: (5 -20) mg/L;2) Deficient: ≤5 mg/L;3) Excess: ≥ 20 mg/L

Basic information: Maternal age; Gestational age; Maternal history; BMI (Body Mass Index): Bodyweight (kg)/Height (m^2)

The patients BMI were classified according to World Health Organization criteria:

Classification	BMI(kg/m^2)
Underweight	<18.5
Normal	18.5 -24.9
Overweight	25.0-29.9
Obese:	
Class 1	30.0-34.9
Class 2	35.0-39.9
Class 3	≥40.0

Sample collection: Fasting samples of all the pregnant women were collected from the peripheral venation, the median cubital vein, 2 mL of the left limb. Each sample was allowed to clot, centrifuged and used as serum

samples for vitamin E analysis. The result was compared with the standard curve to determine Vitamin E level.

Measurements Methods: High-Performance Liquid Chromatography (HPLC). Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

Main reagents and instruments: Vitamin E kits produced by UK PUGI Company. Pre-treatment solution: triethanolamine, methanol buffer. Fully automatic biochemical analyzer: model Ai3200UK PUGI Company.Hydrogen peroxide exitor. Centrifuge: EppendrfCompanyproduces Cryogenic Refrigerator: Haier.

Statistical methods: The collected data were statistically analyzed using SPSS version 20.0 software. The measurements of data are expressed by Mean ±SD and independent t-test. The utilization rate of counting data % indicated that there was statistical significance in Chi-square test (P<0.05)

RESULTS

Basic data of pregnant women: 1910 pregnant women were included in the study. The basic information of the subjects was obtained by using (Mean ±SD).

Group	No. of cases(n)	Age (Years)	Parity	BMI (kg/m^2)	Gestational age(weeks)
Control	1000	30.78±2.08	1.80±0.40	23.28±0.99	34.00±0.99
Gestational hypertension	300	31.54±2.56	1.70±0.45	22.94±0.09	34.39±0.79
Pre -eclampsia	250	31.44±2.39	1.64±0.48	21.86±0.73	33.99±1.05
Severe pre - eclampsia	360	32.50±1.80	1.85±0.35	23.64±0.82	33.56±1.05
F		31.700	0.49	10.341	29.535
P		>0.05	>0.05	>0.05	>0.05

Table 1: A list of the basic conditions of pregnant women (Mean ± SD)

The difference between two groups was analyzed by variance analysis. The result showed that there was no significant difference in age, parity, BMI, of pregnant women and gestational weeks of blood collection in late pregnancy between the groups (P>0.05).

Distribution of Vitamin E in maternal serum in our hospital:

Group	Vitamin E (n=1910)	
	n	%
Normal	1620	84.8%
Abnormal	290	15.2%
Deficient	156	53.8%
Excessive	134	46.2%

Table 2: A list of changes in Vitamin E content in pregnant women in our hospital

Analysis of the correlation between vitamin E and Hypertensive Disorder of Pregnancy:

Group	n	Vitamin E (μgmol/l)
Control	1000	9.88± 0.75
Geatational hypertension	300	8.36± 0.55
Preeclampsia	250	5.55± 0.08
Severe pre eclampsia	360	4.30± 0.50

Table3: A list of Serum Vitamin E levels in Hypertensive Disorder of Pregnancy.

The serum Vitamin E content in the control group and Gestational hypertensive group was mainly normal or high. There was no significant difference between the two groups (t=1.665, *P*=0.096) (*P*>0.05) There was a significant difference between the pre-eclampsia group and severe pre-eclampsia group (t=27.692, *P*=0.000) (*P*<0.05).

Group	No. of cases(n)	Normal		Excessive		Deficient	
		n	%	n	%	n	%
Control	1000	898	89.8	80	8.0	22	2.2
Gestational hypertension	300	250	83.3	26	8.7	24	8.0
Pre-eclampsia	250	190	27.2	20	8.0	40	16.0
Severe pre-eclampsia	360	262	14.4	28	7.8	70	19.4

Table 4: Distribution of Hypertensive Disorder of Pregnancy with vitamin E deficiency

In the deficient group, the proportion of severe pre-eclampsia group was 19.4%. pre-eclampsia group was 16.0%, Gestational Hypertensive group was 8.0% and the control group was the smallest 2.2%.

When vitamin E was excess: There was no significant difference between the control group and Gestational Hypertensive group in pregnancy, pre-eclampsia group, and severe pre-eclampsia group. Significant statistical significance(X^2=0.164, *P*=0.983) *P*>0.05.

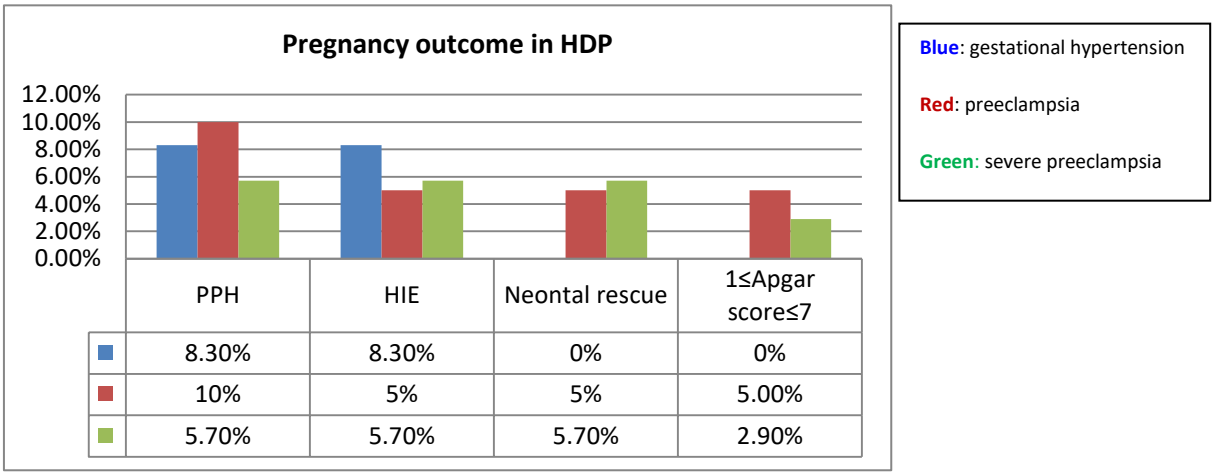
When vitamin E was deficient: The two groups were compared.

There was a significant difference between the control group and Gestational Hypertensive group (X^2=20.580, *P*=0.00) *P*<0.05. There was no significant difference between pre-eclampsia and severe pre-eclampsia group (X^2=0.827, *P*=0.399) *P*>0.05

Group	PPH		HIE		Neonatal rescue		1≤Apgar score≤7	
	n	%	n	%	n	%	n	%
Gestational Hypertensive	2	8.3	2	8.3	0	0.0	0	0.0
Pre-eclampsia	4	10.0	2	5.0	2	5.0	2	5.0
Severe pre-eclampsia	4	5.7	4	5.7	4	5.7	2	2.9

Table 5: Analysis of vitamin E deficiency and pregnancy outcome of Hypertensive Disorder of Pregnancy (n %)

Vitamin E deficiency and pregnancy outcome in Hypertensive Disorder of Pregnancy: We compared the Vitamin E deficiency and Pregnancy outcomes between the Gestational Hypertensive group, pre-eclampsia group, and severe pre-eclampsia group. Common complications in these outcomes were post-partum hemorrhage, hypoxic-ischemic encephalopathy, requiring neonatal rescue and 1≤Apgar Score≤7. (X^2=2.325, P=0.887) (P >0.05). There was no significant difference in the incidence of 1≤Apgar Score≤7 and Neonatal rescue between the pre-eclampsia and the severe pre-eclampsia.



Graph 1: Pregnancy outcomes of vitamin E deficiency Hypertensive Disorder of Pregnancy

DISCUSSION

Pre-eclampsia is a disorder of pregnancy characterized by (≥140 mmHg systolic blood pressure and ≥90 mmHg diastolic blood pressure) and new-onset proteinuria (≥300mg protein/d) occurring in the mid-half of pregnancy [18]. It is life-threatening multi-organ involvement disease and remains the major cause of maternal and neonatal morbidity and mortality [14]. The incidence rate reported worldwide is 5%-12% [15]. Pre-eclampsia is a multi-organ disease and can affect the kidney, liver, brain and the blood clotting system [3,4]. Hypertensive Disorder of Pregnancy can be divided into Pre-eclampsia and severe Pre-eclampsia according to the severity of the disease. Severe preeclampsia is the major and leading cause of maternal and fetal

morbidity and mortality [24].In recent years, perinatal mortality caused by Hypertensive Disorders of Pregnancy has been the first of all complications of pregnancy [16]. This disease not only endangers the safety of pregnant women and fetuses but also has a harmful impact on the future health of mothers and children. People with Hypertensive disorder in pregnancy and their offspring have an increased risk of cardiovascular and cerebrovascular disease in the future [17]. So it is very important to understand the risk factors of its onset, to prevent and intervene as early as possible and to prevent the occurrence of adverse pregnancy outcomes.

This paradox has led to the hypothesis that pre-eclampsia is a two-stage disorder, with reduced placental perfusion representing stage one (Redman 1991), while stage two refers to the multisystemic disorder or maternal syndrome produced in response to reduced placental perfusion that is influenced by genetic or environmental maternal constitutional factors. Oxidative stress suggests the linkage between these two [23]. There is a hypothesis given which predicts that administration of antioxidants would decrease oxidative stress and modify stage- two [23].Endothelial activation appears to be central of the pathophysiological changes associated with pre-eclampsia, with circulating markers of endothelial activation increased in pre-eclampsia and in those women destined to pre-eclampsia.

An abnormal healthy pregnancy is associated with a systemic inflammatory response. Such an inflammatory response can cause or be caused by endothelial dysfunction and oxidative stress.Thus there are increasing pieces of evidence that oxidative stress plays an important role in the pathogenesis of pre eclampsia[9,10] perhaps acting as the link in the two-stage model of pre-eclampsia.

Our data suggest that vitamin E contents may be related to the occurrence of PIH disorders in pregnancy and vitamin E deficiency may be associated with PIH but does not increase the incidence of PIH. According to WHO Database on vitamin E deficiency in pregnant women from the year, 1995-2005 showed that pregnant women in low and middle-income countries worldwide suffer from vitamin E deficiency and has various maternal and perinatal complications [28].

The strength of our study includes its size, its prospective design and the general quality of the data.

Although the debate on the exact role of oxidative stress in the pathophysiology of pre-eclampsia continues[19].increasing evidence suggests that a disruption in oxidative stress- antioxidant balance in pregnancy is likely to contribute to, and the placenta is likely to central to, oxidative stress in pre-eclampsia.

The preliminary study by (Chappell et al.1999), showing a highly-significant (P=0.02) reduction in the incidence of pre-eclampsia in women at risk who take a vitamin E supplement from mid-pregnancy, has provided the strong evidence to date that oxidative stress is implicated in the pathogenesis of pre-eclampsia and that supplementation with antioxidant like vitamin E during pregnancy may prevent or postpone its occurrence.The pieces of evidence suggesting that antioxidant prophylactics in high-risk women have not only lowered the prevalence of pre-eclampsia but also has demonstrated multiple other actions [11] support our study.

Antioxidant supplementation seems to reduce the risk of pre-eclampsia and appears to be a

reduction in the risk of having an SGA associated with antioxidants although there is an increase in the risk of preterm birth [21].

Evidences that there is an increasing evidence that pre-eclampsia is associated with both increased oxidative stress and reduced antioxidant defenses, which has led to hypothesis that oxidative stress may play an important role in the pathogenesis of pre-eclampsia[21,22] and lower levels of vitamin E was observed in preeclamptic women compared to control group (P<0.001)and (P<0.05) also supports our study[25].

According to the WHO Database on vitamin E deficiency in pregnant women from the year, 1995-2005 showed that pregnant women in low and middle-income countries worldwide suffer from vitamin E deficiency and has various maternal and perinatal complications.

CONCLUSION

Vitamin E contents are related to the hypertensive disorder of pregnancy.

Vitamin E deficiency is related to the occurrence of hypertensive disorders of pregnancy and has effects on maternal health and fetal outcomes.

Serum levels of vitamin E detection during pregnancy can help in the prediction of hypertensive disorders of pregnancy**;** hence, it can help to reduce the risk of Pre-eclampsia.

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