

**PREVALENCE, ASSOCIATED FACTORS AND ROLE OF VITAMIN D AND GLUTATHIONE REDUCTASE OF PRE-ECLAMPSIA IN PREGNANT WOMEN**

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**Abstract**

**Introduction:** In maternal and neonatal cases, preeclampsia is a multi-organ, heterogeneous pregnancy condition associated with significant morbidity and mortality. Since preeclampsia is a progressive disease, in some cases, delivery is necessary to stop the progression to the benefit of the mother and foetus. However, the need for early delivery has adverse effects on significant neonatal outcomes that are not limited to the most premature babies. The results include oxidative stress in the disease and invoke the biochemical basis for antioxidant clinical trials to prevent and treat hypertension caused by pregnancy. In the management of preeclampsia, supplementation of antioxidants along with polyunsaturated fatty acids, particularly omega-3 fatty acids, may be useful. This describes vitamin Ds potential role in the pathogenesis of preeclampsia. However, the role of vitamin D supplementation and dosing is controversial in preventing preeclampsia.

**Method:** The study was carried out from March 2019 to April 2020 at Shalinitai Meghe Hospital and Research Centre using institutional-based cross-sectional study design among women whose age was greater than or equal to eighteen. Data were collected using a standardised and pretested questionnaire from 150 participants by face-to-face interview technique. Using Chemiluminiscent Immunoassay (CLIA), vitamin D estimation was performed. The behaviour of Glutathione Reductase was calculated according to the Goldberg et al 1983 procedure. To classify the factors associated with the development of preeclampsia, logistic regression analysis was used.

**Result:** With a mean age of 30.28, a total of 150 participants were enrolled in the study. Evaluation of vitamin D and glutathione levels The prevalence of preeclampsia among current pregnant women attending ANC at Shalinitai Meghe Hospital was 16 with a 95 % CI. The current preeclampsia was significantly correlated with predictive variables such as the age of the respondents, current multiple pregnancy, and history of diabetes mellitus.

**Conclusion:** The findings of this study showed that preeclampsia was present in a large proportion of women. For both urban and rural residents, health seeking actions towards pregnant women should be promoted, offering an opportunity to detect preeclampsia as early as possible and preventing the coming complication of preeclampsia. The role of antioxidants is controversial in the prevention of preeclampsia. Vitamin D deficiency is associated with preeclampsia in a major way. To document the role of vitamin D supplementation in the prevention of preeclampsia, further studies are required.

**Keywords:** Gestational hypertension, Pre-eclampsia, Vitamin D, GSH

**Introduction**

Preeclampsia is the world's leading cause of maternal and perinatal morbidity and mortality, and it is a hypertensive condition that typically occurs 20 weeks after childbirth. This is a rapidly progressive disease characterised by high blood pressure and urinary protein [1, 2]. It is a source of serious morbidity both in mothers and their infants, long-term disability and death. The risk of maternal mortality is much more likely in settings where pregnant women are not regularly available for prenatal and intrapartum care[3].

Around 830 women died every day in 2015 due to pregnancy and childbirth complications. Nearly all of these deaths occurred in low-resource areas, and most of them could have been avoided[4]. One of the major causes of death is hypertension caused by pregnancy, such as

preeclampsia [5 , 6]. In Sub-Saharan Africa, 550 of the 830 daily maternal deaths occurred and 180 in Southern Asia, compared to 5 in developed countries. The risk of a woman dying from maternal-related causes in a developing country during her lifetime is around 33 times greater compared to a woman living in a developed country[7].

In developed countries, preeclampsia prevalence ranges from 1.8 percent to 16.7 percent[8]. For example, in 10 percent of pregnancies in African women, the prevalence of preeclampsia occurs, which is substantially greater than the global average of about 2 percent[9].

The incidence of preeclampsia among pregnant women in India is estimated to be 8-10 per cent. The prevalence of hypertensive pregnancy disorders in 5.4 percent of the

study population in India was 7.8 percent with preeclampsia, according to a study. [10]

It is known that vitamin D has anti-inflammatory effects, and there is evidence of an inverse association between calcium dietary intake and Preeclampsia incidence. In this article, evidence of the role of vitamin D status and supplementation in Preeclampsia aetiology and prevention is reviewed along with the identification of research gaps to inform future studies.[11]

Enzymatic antioxidant glutathione reductase (GSH), which limits the cellular concentration of free radicals and prevents excessive oxidative damage, are the free radical scavenging mechanisms. Until recently, there has been insufficient evidence supporting the effectiveness of vitamin C and vitamin E supplementation in preventing preeclampsia.[12]

The problem is confounded by the continuing uncertainty of aetiology and the uncertain existence of the disease[13]. The goal of this paper is, therefore, to highlight the challenges of combating the successful management of preeclampsia in developing countries and to recommend steps that could be used in the local context to resolve them.

Despite the adverse effects of this condition on maternal and child health[14], its prevalence remains high, especially in developing countries, including India. In general, both maternal and child morbidity and mortality are still a big issue with preeclampsia. This research will therefore evaluate the prevalence levels of vitamin D and glutathione and their related preeclampsia factors among pregnant women.

## Methods

### Study design, period and population

From March 2019 to April 2020, institutional-based cross-sectional research design was conducted among women whose age was greater than or equal to eighteen. It included selected pregnant women who had given birth to at least one child and those over 20 weeks of gestation for the current pregnancy.

### Inclusion criteria

- All pregnant women attending department of obstetrics and gynecology who were diagnosed as hypertensive disorders of pregnancy were taken for this study.

### Exclusion criteria

- Patients diagnosed with other causes of convulsion were excluded in this study.

## Sampling procedure and data collection instrument

First, we obtained the annual report in ANC of pregnant mothers with gestational age greater than 20 weeks, then we split by 12 to get the flow per month of pregnant mothers. Then we eventually noticed about 175 pregnant mothers coming for follow-up with the ANC. Then, within the specified period, the total sample size needed was consecutively collected.

Different literature and scientific evidence are checked and the questionnaire is adopted and modified[16,17,18]. Data were collected using a standardised and pretested questionnaire using a face-to-face interview technique. For certain clinical and laboratory effects, including proteinuria and measurement of blood pressure, medical reports were also checked.

Venous blood samples were collected after 12 hr overnight fasting for 25(OH)Vitamin D estimate, shielded from light, centrifuged and processed at  $-20^{\circ}\text{C}$  until review. The Chemiluminiscent Immunoassay (CLIA) was used to estimate 25(OH) Vitamin D. The value of 25(OH) Vitamin D  $\leq 20$  ng / ml was cut off to assess vitamin D deficiency. Using the Pearson Chi-Square test to compare categorical variables

**Glutathione reductase (GSH):** Activity of Glutathione reductase was calculated according to the Goldberg et al 1983 method. In the presence of NADPH, which is oxidised to NADP<sup>+</sup>, Glutathione Reductase catalyses the reduction of glutathione. The decrease in absorbance is estimated at 340 nm. [19]

## Data processing and analysis

Data was entered using the epi-data manager and exported, cleaned and analysed using version 21 of the Social Science Statistical Package (SPSS).

Multicollinearity was tested between the variables and there was no interaction between independent variables. The linear relationship between the continuous variable age and its logit transformation was also verified and finally we discovered that there was no linear relationship. As a result, the age of the independent variable was listed. Using the bivariate logistic regression model, each independent / predictor variables and outcome variable were researched. In the multivariate logistic regression model, the independent variables that were statistically significant with p value  $< 0.05$  and 95 percent CI in bivariate analysis were used using the enter method to control possible confounder variables. Finally, as good predictor variables of preeclampsia, variables (age, current multiple pregnancy and participant history of diabetic mellitus) with a p value  $< 0.05$  were taken.

## Ethical consideration

A letter of approval from the institutional ethical committee was received. For each participant, the appropriate details concerning the relevance of the study was discussed. Each participant obtained written consent and retained their confidentiality and privacy.

## RESULT

A total of 150 participants who came to Shalinitai Meghe hospital for ANC follow-up were enrolled in the study with a 100 % response rate. The mean age of the respondents was 30.28. Of the participants, about 47 (38.4 %) and 37 (30.7 %) were in the 25-29 and 30-34 age range, respectively.

Of the participants, 113 (87.6 %) were married, and 50 (38.7 %) were religiously Protestant. By their occupational status, more than half of the participants, 78 (60.4 %) were housewives, while 19 (14.0 %) of the respondents never had more than one partner.

From March 2019 to April 2020, over a period of one year, a total of 500 pregnant women visited the ante-natal clinic. 150 of these cases were diagnosed with hypertensive pregnancy disorders.

**Table 1:** Vitamin D and Glutathione status & severity of preeclampsia

Vitamin D (ng/ml)	mild preeclampsia No. of cases	Severe preeclampsia No. of cases	Mean vitamin D and Mean GSH
<20(deficient)	55	40	26.97 ± 3.70
>20(normal)	23	32	29.74 ± 5.82
GSH (IU/gmHb)	85	65	35.81±8.7

**Table 2:** Prevalence of hypertensive disorders

Types of hypertensive disorders	No. of cases	%
Gestational hypertension	25	16.6
Pre-eclampsia	75	50
Chronic hypertension	25	16.6
Pre-eclampsia superimposed on chronic hypertension	25	16.6

Table 2 shows prevalence of hypertensive disorders in which gestational hypertension (16.6%) was most common followed by pre-eclampsia (50%), pre-eclampsia superimposed on chronic hypertension (16.6%) and chronic hypertension (16.6%).

**Table 3:** Age distribution of cases

Maternal age (in years)	Number of cases	%
18-22	35	23.3%
23-27	37	24.6%
28-32	28	18.6%
> 33	50	33.3%

Table 3 shows age distribution of cases, in which hypertensive disorders were highest in the age group of >33 years of age (33.3%) followed by 24.6% of patients in the age group of 23-27 years of age, 18.6% of patients in

the age group of 28-32 years of age and 23.3% of patients in the age group of 18-22 years of age.

**Table 4:** Gravida wise distribution

Gravidity status	Number of cases	%
primi	85	56.6%
Multi	65	43.3%

Table 4 shows gravida wise distribution, majority were seen among primi-gravida (56.6%) than multi-gravida (43.3%).

## Factors associated with preeclampsia

In bivariate study, different independent variables such as: age, residence, ever had more than one spouse, current multiple pregnancy, family history of diabetes mellitus, participant history of diabetes mellitus, participant history of kidney disease, prior pregnancy history of ANC follow-up, and parity was significantly correlated with preeclampsia mothers. However, variables like age, current multiple pregnancy and participant history of diabetic mellitus have become strong independent predictor variables for preeclampsia after correcting for the potential confounding factors utilising multivariate analysis.

## Discussion

Hypertensive pregnancy conditions have the most adverse effect on both the mother and the foetus. One of the key public health issues responsible for rising maternal and perinatal morbidity and mortality is this disease. Primary paternity, maternal age extremes, multifetal childbirth, and births by assisted reproductive methods, pre-eclampsia in prior births, renal dysfunction, connective tissue disorders, and pre-eclampsia family history are some of the risk factors for preeclampsia. During pregnancy, smoking decreases the risk of hypertension.[20] Failure of the second wave of cyto-trophoblastic invasion of spiral arterioles in the muscular layer is the primary cause behind pre-eclampsia. Other factors include maternal, placental and foetal tissue immunological intolerance, maternal maladaptation to normal pregnancy to inflammatory or cardiovascular changes, and genetic influences.

Compared to Bodnar et al.[21] (65 percent) and Ullah et al.[22] (78.19 percent), the prevalence of vitamin D deficiency in this research is 69 percent. The mean level of vitamin D in women with preeclampsia in our sample was significantly low. Mean vitamin D was significantly lower in the mid-trimester preeclampsia population and, when adjusted for other parameters, the decrease in serum vitamin D concentrations < 30 ng / ml doubled the risk of preeclampsia [21]. There was a 3-5 fold rise in the incidence of preeclampsia associated with vitamin D deficiency[22]. Contrary to several other studies, comparable levels of vitamin D were found in controls and

in pre-eclamptic women [23, 24]. However, the severity of vitamin D deficiency in our sample did not correlate with the severity of preeclampsia. Similar findings were made by Singla R et al.[25] On the contrary, others reported a positive association between hypovitaminosis D and preeclampsia severity[21, 22].

The oxidant / antioxidant balance is tipped in favour of oxidants at the cost of antioxidants in preeclampsia, since elevated maternal lipid peroxide levels have been measured in plasma. The first line of protection against ROS is antioxidant enzymes such as Superoxide Dismutase, Glutathione Peroxidase, and Glutathione Reductase, and the reduction in their activities leads to the oxidant attack on the cells. The results include oxidative stress in the disease and invoke the biochemical basis for antioxidant clinical trials to prevent and treat hypertension caused by pregnancy. In the management of preeclampsia, supplementation of antioxidants along with polyunsaturated fatty acids, particularly omega-3 fatty acids, may be useful. 26. [26]

In this study, the total prevalence of pregnancy hypertensive disorders was 10.4 percent, in 25 cases gestational hypertension was diagnosed (16.6 percent), in 45 cases pre-eclampsia (50 percent), in 25 cases chronic hypertension (16.6 percent), in 25 cases extreme pre-eclampsia superimposed on chronic hypertension (16.6 percent). India's prevalence of pre-eclampsia in hospital practise ranges from 5-15% and around 1.5% for eclampsia. [27] The prevalence of PIH was 10.7 percent for primi-para and 9.1 percent for multi-para, stated by Bindu K et al. [28] In the current sample, the incidence was 23.3 percent in the 18-22 age group, and 24.6 percent in the 23-27 age group. The highest incidence of hypertensive disorders among the 23-27 age group occurred in the Gogaram et al report. [29] The prevalence of primigravida was highest in our sample (56%) compared with multigravida (43.3 percent). In their research, Kolluru V et al, recorded that the incidence of hypertensive disorders in primigravida was 48.3% and multigravida was 50.9%. [30]

Maternal age was found to be substantially correlated with preeclampsia in this study. Respondents whose age was less than or equal to 24 were less likely than those whose age was greater than or equal to 35 to be pre-eclamptic women. This is in line with the research carried out in Germany[31], Pakistan[32], Tehran, Iran[33] and India[15]. This could be clarified by growing age, blocking the arteries, which could lead to significant consequences such as strokes or heart attacks. As age increases, the body's diet or lack of exercise and ability to absorb dietary salt may be low, which in turn causes decreased blood vessel elasticity and eventually causes women to be hypertensive. [34]

Preeclampsia has also been greatly correlated with multiple gestations. In this study, respondents who did not have multiple pregnancies were less likely than women with multiple pregnancies to be pre-eclamptic. The results of the research were consistent with those of studies performed in Egypt[35] and Ireland[36]. This may be due to the fact that, by antagonising placental growth factor and vascular endothelial growth factor signalling in the maternal vasculature, preeclampsia is associated with the presence of a soluble agent that is a circulating antiangiogenic molecule of placental origin, playing a central role in preeclampsia[37].

### Conclusion

In this study, the prevalence of preeclampsia was higher than in other related trials. Factors associated with preeclampsia were the age of the participant, having multiple pregnancies and having a history of diabetes. The biggest health issue is hypertensive pregnancy disorders, which are the primary cause of maternal morbidity and mortality. It is not possible to prevent gestational hypertension, but pre-eclampsia development and its complications can be avoided by early diagnosis and careful treatment, thus decreasing maternal morbidity and mortality.

Our study shows that vitamin D deficiency is associated with preeclampsia in pregnancy. This result is also confirmed by most of the published evidence. But there is no question that the role of vitamin D supplementation in the prevention of preeclampsia is not confirmed. Based on the findings of the current research, it is evident that there is an altered oxidant status in PIH and a reduced antioxidant enzyme status, implying that there is indirect evidence of oxidative stress in pre-eclampsia. Our study found that the combination of Vitamin E with Omega 3 fatty acids during preeclampsia by supplementing women with antioxidants can help to counteract oxidative stress and thus prevent or delay the onset of preeclampsia, thereby improving the mother's and baby's health. Early identification of cases along with early initiation of anti-hypertensive drugs to resolve adverse maternal outcomes by adequate antenatal checkup at all levels of health care.

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