

Original Research Article

Significance of 25 Hydroxy Vitamin D and Calcium in Pregnancy Induced Hypertension

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ABSTRACT

Background: Pregnancy induced hypertension (PIH) is a common gestational disorder which complicates 7-10% of pregnancies globally and it is associated with maternal, fetal and neonatal morbidity and mortality. Yet the etiology of this disorder is little understood. Alterations in Vitamin D and serum calcium (Ca) levels have been suggested as effective factors in causing PIH.

Aim: To evaluate levels of 25 hydroxy vitamin D and calcium in pregnancy induced hypertension.

Materials And Methods: The study was conducted on 50 patients with pregnancy induced hypertension with 40 pre eclamptic women and 10 eclamptic women (study group) and 50 normal pregnant women (control group) in the Department of Biochemistry, Government Medical College Patiala. Sample was collected in plain vial. Serum 25-hydroxy vitamin D and calcium levels were evaluated by ELISA technique and OCPC colorimetric method respectively and the data obtained was statistically analysed.

Results: The Mean values of serum 25-hydroxyvitamin D levels in study group and control group were 9.83 ± 6.11 ng/ml and 14.92 ± 3.35 ng/ml respectively (Normal Value of vitamin D =30-74 ng/ml). The mean values of serum calcium in study group and control group were 8.76 ± 1.12 mg% and 9.48 ± 0.93 mg% respectively (normal value of calcium =8.5 to 10 mg%). The decrease in Vitamin D levels in study group as compared to control group shows statistically significant association (p value < 0.04). Similarly decrease in calcium levels among study group in comparison to control group shows statistically significant association (p < 0.01).

Keywords: Pregnancy induced hypertension, Pre eclampsia, Eclampsia, 25 Hydroxy Vitamin D, Serum Calcium

INTRODUCTION

Pregnancy induced hypertension (PIH) is defined as the hypertension that develops as a direct result of the gravid state. It can be classified as Gestational hypertension, Pre-eclampsia (PE) and eclampsia syndrome. [1] Pregnancy establishment and implantation depend on the harmonious confluence of complex molecular events related to angiogenesis, hormone production, and inflammation. Multiple factors, such as maternal

constitutional factors, angiogenetic factors, endothelial dysfunction, syncytiotrophoblastic microparticles (STMP), and inflammatory activation, play a role in the development and progression of preeclampsia. [2] Various epidemiological studies have emphasized the role of vitamin D deficiency in the development of PIH. [3]

Calcium homeostasis is an important aspect of maternal and fetal physiology during gestation, and recent evidence implicates alterations in calcium metabolism

in the pathogenesis of hypertension during pregnancy. Deficiencies in calcium intake have been linked to preeclampsia/eclampsia, and hypocalciuria and deviations in both 1,25(OH)2D3 and PTH have been shown in women with preeclampsia. [4] Preliminary studies also suggest that calcium supplementation may lower blood pressure and prevent preeclampsia in pregnant women. [5]

The recommendation of calcium supplementation for individuals with decreased calcium intake to prevent and treat PE by the World Health Organization (WHO) has increased the popularity of calcium and vitamin D trials in particular. [6] Our study also aimed to investigate the serum vitamin D and calcium levels in eclampsia, preeclampsia and healthy pregnant women and to assess its role in the etiology of PE and eclampsia.

MATERIALS AND METHODS

Hospital based observational comparative study was conducted in Department of Biochemistry, Rajindra Hospital, Patiala on 50 patients with pregnancy induced hypertension with 40 pre eclamptic women and 10 eclamptic women (study group) and 50 normal pregnant women (control group).

The diagnosis of preeclampsia was confirmed using the "Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy" criteria. Based on these criteria, patients with systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg (measured after a period of rest of four hours, twice daily) and proteinuria (≥ 300 mg protein/24 h) were diagnosed as preeclampsia. The diagnosis of eclampsia was based on the presence of tonic-clonic seizures in patients that were followed up with the diagnosis of preeclampsia with no systemic disease that may cause seizures. [1]

Inclusion Criteria included Pregnant females with upto 35 years of age and with gestation 20 weeks or more.

Exclusion criteria included all cases of previous history of essential hypertension or chronic hypertension due to any other cause, any associated renal, hepatic, cardiac or neurological disorders not due to pregnancy induced hypertension, known cases of diabetes mellitus type 1 and 2, PCOS, associated molar pregnancy and multiple pregnancy.

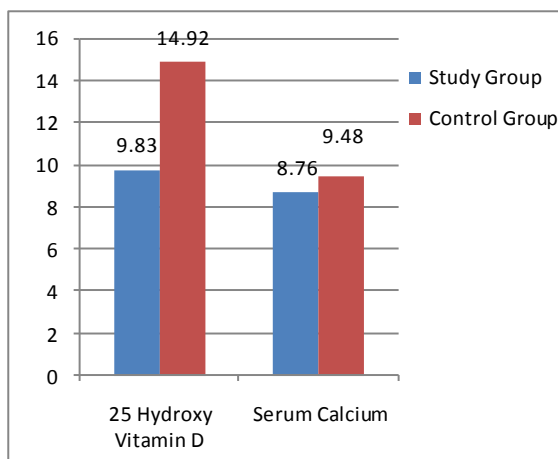
Blood Samples obtained from both groups were collected in plain vacutainers. 25 Hydroxy Vitamin D levels and serum calcium levels were measured by ELISA method and OCPC method respectively. Results obtained were statistically analyzed using student t-test. A p-value less than 0.05 was considered significant.

RESULT

No statistically significant differences were found in age, gravidity, parity, weight and height among the demographic data between the groups. Systolic and diastolic blood pressures were significantly higher in the eclamptic and pre eclamptic patient groups compared to the healthy pregnant women ($P < 0.001$ and $P < 0.001$, respectively). The Mean values of serum 25-hydroxyvitamin D levels in study group and control group were 9.83 ± 6.11 ng/ml and 14.92 ± 3.35 ng/ml respectively (Normal Value of vitamin D = 30-74 ng/ml). The mean values of serum calcium in study group and control group were 8.76 ± 1.12 mg% and 9.48 ± 0.93 mg% respectively (Normal value of Calcium = 8.5 to 10 mg%). The decrease in Vitamin D levels in study group as compared to control group shows statistically significant association (p value = 0.04). Similarly decrease in calcium levels among study group in comparison to control group shows statistically significant association ($p < 0.01$).

Table 1 shows result after data was analysed statistically

Parameters	Study group	Control group	P value	Significance
25- Hydroxy Vitamin D (ng/ml)	9.83 ± 6.11	14.92 ± 3.35	0.04	S (significant)
Serum Calcium (mg%)	8.76 ± 1.12	9.48 ± 0.93	< 0.01	S



DISCUSSION

Vitamin D insufficiency has been associated with several adverse health outcomes, including pregnancy outcomes, and is increasingly recognized as a public health concern. It is responsible for approximately 50,000 maternal deaths yearly worldwide, 25% of all cases of fetal growth restriction, and 15% of preterm births in developed countries [7]. Observational data suggest a link between low 25-hydroxyvitamin D (25(OH) D) levels - the best measure of vitamin D status in humans - and an increased risk of adverse pregnancy outcomes such as gestational diabetes, pregnancy induced hypertension and fetal growth restriction. [3]

In the present study, the 25 Hydroxy Vitamin D levels in the study group were 9.83 ± 6.11 ng/ml and in the control group were 14.92 ± 3.35 ng/ml. The p value was 0.04 which was statistically significant. (Table 1)

Similar results showing significant relation have been concluded by Wei et al [3] (2012) Tara gupta et al [8] and Ullah MI et al [9] ($p < 0.05$). 25 Hydroxy Vitamin D levels were very low in PIH cases i.e $p < 0.001$ in accordance with studies conducted by Robinson CJ et al [10] (2010), Baker AM et al [11] (2010), Singla R et al [12] (2014) and Ringrose JS [13] (2011). Singla et al [12] (2014) also found that there was no difference in vitamin D level of women with eclampsia ($p = 0.956$) or imminent eclampsia ($p = 0.310$) and those without these complications. They concluded that

there is high prevalence of vitamin D deficiency among pregnant women in India. Women with preeclampsia had significantly lower vitamin D level as compared to normal women. However, severity of the disease was not related to vitamin D level.

In contrast, Wetta LA et al [14] (2014) and Burris HH et al [15] (2014) conducted studies which does not support the hypothesis that mid trimester maternal vitamin D was significantly associated with preeclampsia.

Results drawn by Harinarayan et al [16] (2009) showed that 25 Hydroxy Vitamin D levels among adult females in urban and rural areas were 15.5 ± 0.3 ng/ml and 19.0 ± 0.89 ng/ml respectively. Hence, inference can be drawn that 25 hydroxy Vitamin D levels does not alter in normal pregnancy and its deficiency is prevalent in all types of sample group. However, pre- eclamptic and eclamptic women have severe Vitamin D deficiency (9.77 ± 6.69 ng/ml).

There is evidence that vitamin D affects transcription and function of genes responsible for trophoblast invasion, angiogenesis critical for implantation, and fetal allograft immunologic "tolerance". Through actions in these domains, vitamin D may be an important factor in preeclampsia causation. [2] Moreover, role of Vitamin D as negative endocrine regulator of Renin angiotensin system (RAS) cannot be repudiated. An important aspect of vitamin D pleiotropic effects is the interaction between receptors of vitamin D (VDR) and the components of RAS. Vitamin D reduces plasma renin activity, angiotensin II (Ang II) and myocardial hypertrophy. An inverse association of circulating vitamin D levels with blood pressure has been demonstrated and it has been shown that the treatment with vitamin D analogues reduces blood pressure. [17]

Moreover, the serum calcium levels in the study group were 8.76 mg% and in the control group were 9.48 mg%. The p value was < 0.01 which was statistically significant. (Table 1)

Similar results showing significant relation have been concluded by Punthumapol C et al [18] (2008) ($p < 0.05$). Calcium levels were very low in PIH cases i.e. $p < 0.001$ in accordance with studies conducted by Sukonpan K et al [19] (2005), Kumar A et al [20] (2009), Kanagal DV et al [21] (2014).

A probable theory to this observation may be that when serum calcium levels are decreased, the levels of intracellular calcium are increased, leading to constriction of smooth muscles in blood vessels and therefore increased vascular resistance, culminating in a raised systolic and diastolic blood pressure. Furthermore, previous reports suggest that altered calcium homeostasis, as exhibited by increased calcium excretion, is associated with higher blood pressure levels. Low serum calcium levels may also increase blood pressure by stimulating parathyroid hormone and renin release, which in turn increases intracellular calcium in smooth muscle, leading to vasoconstriction. This implies that calcium levels may play a role in hypertensive disorders in pregnancy. [22,23] Our result is not in keeping with that of Trumbo PR et al [24] (2007) who reported that the relationship between calcium and risk of pregnancy-induced hypertension is highly unlikely, inconsistent and inconclusive. Socioeconomic status may be correlated with calcium intake. Low-income women of reproductive age were more likely to have less than the recommended dietary allowance for calcium.

Our study revealed that the vitamin D and calcium levels were significantly lower in patients with PE and eclampsia compared to the healthy pregnant women. In addition, our study revealed that vitamin D levels were similar in the PE and eclamptic groups.

Dietary patterns were not determined, thus the impact of inadequate intake of these elements as the possible confounding effect remains. Findings from the study however remain relevant and add to evidence on the subject matter.

CONCLUSION

From the present study, it was concluded that 25 Hydroxy Vitamin D and calcium levels were lowered in patients of pregnancy induced hypertension as compared to normotensive pregnant women.

Early detection of deficiencies of these parameters (both prior to conception or in early period of pregnancy and in females having previous history of PIH) may be helpful in preventing occurrence of PIH. So, this study conveys the message that predictive and prognostic value of these parameters may be helpful in the early diagnosis of PIH. All these endeavors may contribute to alleviate maternal morbidity and preterm birth outcomes.

Proper guidance to pregnant women (both having previous history of PIH or in early period of pregnancy) regarding dietary modifications by including Vitamin D and calcium rich food sources, may be beneficial in preventing PIH occurrence. Moreover, it may decrease burden on health care set up esp, in developing countries where medical facilities can be channelized to tackle other major health concerns among populations.

How much decline in levels of 25 - hydroxy Vitamin D and calcium are associated with an increased risk of hypertension in pregnancy? At what stage do these changes begin to manifest as a rise in blood pressure and proteinuria. Further studies among larger and different population are required to add to the existing matter.

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