SERUM 25 (OH) VITAMIN D AND CALCIUM LEVELS AND ADVERSE MATERNAL AND PERINATAL OUTCOMES IN PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

Objectives: Incidence of hypertensive disorders in pregnancy is about 5–10% of all pregnancies [1]. Pre-eclampsia alone or superimposed on chronic hypertension is the most threatening. This study is done to evaluate the levels of serum 25 (OH) Vitamin D and Calcium in normal antenatal patients and patients with pregnancy-induced hypertension and their effects on perinatal and maternal outcome. Hence, that timely intervention can prevent adverse perinatal and maternal outcomes.

Methods: The present prospective observational study was done in the Department of Obstetrics and Gynecology, Government Medical College and Rajindra Hospital, Patiala, Punjab, India from May 2018 to April 2019. The study was conducted on 80 antenatal patients. Patients were divided into two groups with 40 patients in each group. Group I included patients with pregnancy-induced hypertension and Group II included normal antenatal patients. Serum levels of calcium and 25 (OH) Vitamin D were evaluated in both groups. Adverse perinatal and maternal outcomes were assessed in relation to the serum levels of calcium and 25 (OH) Vitamin D in patients with pregnancy-induced hypertension and normal antenatal patients. Categorical variables were analyzed by Chi-square test and Fisher's exact test. The analysis of continuous variable was done by ANOVA. The data were analyzed using SPSS version 22 and Microsoft Excel. $p \leq 0.05$ is taken as statistically significant.

Results: The mean value of serum Vitamin D level in Group I was 22.30±6.11 ng/ml and 36.68±9.34 ng/ml in Group II giving p=0.016 which was highly significant. In Group I, mean calcium levels were 8.58±0.63 mg/dl and 9.27±0.40 mg/dl in Group II giving p=0.018 which was highly significant. The Pearson's correlation coefficient was −0.753 for serum Vitamin D and systolic blood pressure (BP) and the same for serum Vitamin D and diastolic BP with p=0.001 which was highly significant. The Pearson correlation coefficient was −0.537, −0.514 for serum calcium and systolic BP and serum calcium and diastolic BP, respectively, giving p=0.001.

Conclusion: Serum levels of 25 (OH) Vitamin D and calcium have a significant relationship with pregnancy-induced hypertension. Low levels of calcium and 25 (OH) Vitamin D cause an increased risk of pregnancy-induced hypertension and supplementation of these reduces the incidence of pregnancy-induced hypertension. Hence, their supplementation can be used as a possible intervention strategy in preventing one of the most common causes of perinatal and maternal morbidity and mortality around the world.

Keywords: Pregnancy-induced hypertension, Serum calcium, Serum 25 (OH) Vitamin D.

INTRODUCTION

Incidence of hypertensive disorders in pregnancy is about 5–10% of all pregnancies [1]. Pre-eclampsia alone or superimposed on chronic hypertension is the most threatening. Pre-eclampsia is a multisystem, multifactorial pregnancy-specific syndrome, characterized by high blood pressure and proteinuria after 20 weeks of gestation [1]. It complicates 2.8% of all pregnancies, accounts for 25% of all maternal deaths [2]. The pathogenesis of pre-eclampsia is a two-stage disorder. Stage I is poor placentation caused by faulty endovascular trophoblastic remodeling. Stage II is inflammation, which can be modified by pre-existing maternal condition [3]. Recent studies draw attention on the role of calcium and Vitamin D deficiency in the emergence of pregnancy-induced hypertension.

On exposure to ultraviolet light pre-Vitamin D results in the formation of Vitamin D in the skin. In Liver, Vitamin D gets converted to 25-hydroxy Vitamin D (25 (OH) Vitamin D). Levels of 25 (OH) Vitamin D are evaluated in the body. It transforms to 1,25 di hydroxy Vitamin D which is an active metabolite [4]. 1,25 di hydroxy Vitamin D is considered as pregnancy-supporting factor that works through the direct influence on implantation, placental invasion, and angiogenesis. It also directly affects the immune responses by dendritic cells and macrophages at the fetal placental interface [4]. The decrease in serum calcium levels causes hypertension by stimulating the release of renin and parathyroid hormones. These hormones increase the intracellular concentration of calcium in vascular smooth muscle cells. This leads to vasoconstriction and increased peripheral vascular resistance, culminating in raised blood pressure [5].

Pregnancy is a normal physiological phenomenon with many biochemical changes ranging from an alteration in electrolyte concentrations to more complex changes in 1,25 di-hydroxy Vitamin D and calcium metabolism [5]. This study is done to evaluate the levels of serum Vitamin D and calcium in normal antenatal patients and patients with pregnancy-induced hypertension and their effects on perinatal and maternal outcome in the form of mean gestational age, mean birth weight, ARDS (acute respiratory distress syndrome), APGAR (Appearance, Pulse, Grimace, Activity, and Respiration) <7 at 5 min, fetal growth restriction (FGR), perinatal mortality, eclampsia, and maternal mortality were assessed.

Objectives

The objective of the study was to evaluate levels of 25 (OH) Vitamin D and Calcium in pregnancy-induced hypertension and normal healthy antenatal patients and their effects on perinatal and maternal outcomes.

Table 1: Demographic profile of patients

Parameters	Group I (n=40)	Group II (n=40)	p-value	Name of test
Mean Age (in years) (Mean±SD)	23.23±1.78	26.50±1.30	0.696 NS	Fisher's Exact test
Parity (%)				
Primi	22 (55)	18 (45)	0.324 NS	Fisher's exact test
Multi	18 (45)	22 (55)		

NS: Non-significant

Table 2: Levels of blood pressure, serum 25 (OH) Vitamin D, serum calcium

Parameters	Group I (n=40)	Group II (n=40)	p-value	Name of test
Blood Pressure (mmHg) (Mean±SD)				
Systolic blood pressure	158.60±6.49	119.60±3.28	0.003 HS	Bartlett's test
Diastolic blood pressure	110.00±5.11	79.50±2.66	0.003 HS	Bartlett's test
Serum 25 (OH) Vitamin D (ng/ml)				
<20	23 (57.50%)	4 (10.00%)	0.016 HS	Bartlett's test
21–29	13 (32.50%)	10 (25.00%)		
>30	4 (10.00%)	26 (65.00%)		
(Mean±SD)	22.30±6.11	36.68±9.34		
Serum Calcium (mg/dl)				
<8.5	21 (52.5%)	8 (20.00%)	0.018 HS	Bartlett's test
>8.5	19 (47.5%)	32 (80.00%)		
(Mean±SD)	8.58±0.63	9.27±0.40		

HS: Highly Significant

METHODS

This was a prospective observational study done in the Department of Obstetrics and Gynecology of Government Medical College and Rajindra Hospital Patiala, Punjab, India from May 2018 to April 2019. The ethical committee clearance was obtained from the Ethical committee of Government Medical College and Hospital.

Inclusion criteria

A total of 80 antenatal patients with singleton pregnancies were included in the study. Antenatal patients with pregnancy-induced hypertension, Normal antenatal patients without pregnancy-induced hypertension, and antenatal patients willing to participate in the study were included in the study.

Exclusion criteria

Antenatal patients with other comorbidities were excluded from the study.

Study procedure

Eighty antenatal patients were included in the study.

They were divided into two groups.

Group-I (40 patients) antenatal patients with pregnancy-induced hypertension.

Group-II (40 patients) normal antenatal patients.

After the selection of patients, patients had undergone investigations.

1. 25 (OH) Vitamin D levels (ng/ml) [6].
Sufficient	30–100
Insufficient	21–29
Deficiency	<21

2. Serum calcium levels (mg/dl) [6].
   Normal 8.5 to 10.5 mg/dl.

The patients were followed up throughout their antenatal period till delivery. The serum levels of calcium and 25 (OH) Vitamin D were evaluated and their effects on perinatal and maternal outcomes were studied.

Table 3: Correlation of serum calcium and vitamin D levels with blood pressure

Parameter	Pearson's Correlation co efficient	p-value
Serum Vitamin D and Systolic BP	−0.753	0.001 HS
Serum Vitamin D and Diastolic BP	−0.753	0.001 HS
Serum Calcium level and systolic BP	−0.537	0.001 HS
Serum Calcium level and diastolic BP	−0.514	0.001 HS

HS: Highly significant, BP: Blood pressure

Statistical analysis

The analysis of categorical variables was done by Chi-square test and Fisher exact test. The analysis of continuous variables was done by ANOVA. The data were analyzed using SPSS version 22 and Microsoft Excel. A p≤0.05 was taken as statistically significant.

RESULTS

Mean age of patients in Group I was 23.23±1.78 years as compared to 26.50±1.30 years in Group II giving rise to p=0.696 which was non-significant. About 55% of patients of Group I were primi gravida as compare to 45% of patients in Group II were primigravida giving p=0.324 which was non-significant (Table 1).

Mean systolic blood pressure (BP) in Group I patients was 158.60±6.49 mm Hg as compared to 119.60±3.28 mm Hg in Group II patients giving p=0.003 which was highly significant. Mean diastolic BP in Group I patients was 110.00±5.11 mm Hg and 79.50±2.66 mm Hg in Group II patients giving p=0.003 which was highly significant. Mean serum Vitamin D level of Group I patients was 22.30±6.11 ng/ml and Group II patients were 36.38±9.34 ng/ml giving p=0.016 which was highly significant. Mean serum calcium level of Group I patients was 8.58±0.63 mg/dl and Group II patients was 9.27±0.40 mg/dl giving p=0.018 which was highly significant (Table 2).

There was a negative correlation of serum Vitamin D and serum calcium levels with increased systolic blood pressure and diastolic blood pressure giving p=0.001 for both, which was highly significant. As

Table 4: Perinatal outcomes

Parameter	Group I	Group II	p-value	Name of the test
Mean gestational age (in weeks) (Mean±SD)	36.34±2.64	38.26±1.64	0.001 HS	ANOVA Test
Mean birth weight (in g) (Mean±SD)	2150.24±314.82	2787.60±233.15	0.001 HS	ANOVA Test
ARDS (%)	5 (12.5)	0	0.001 HS	Fisher Exact Test
APGAR <7 at 5 min (%)	9 (22.5)	1 (2.5)	0.001 HS	Fisher Exact Test
Admission to NICU (%)	13 (32.5)	1 (2.5)	0.001 HS	Fisher Exact Test
FGR (%)	11 (27.5)	2 (5)	0.001 HS	Fisher Exact Test
Perinatal Mortality (%)	2 (5)	0	0.01 HS	Fisher Exact Test

ARDS: Acute respiratory distress syndrome, APGAR: Appearance, pulse, grimace, activity and respiration, NICU: Neonatal intensive care unit, FGR: Fetal growth restriction

Table 5: Maternal outcomes

Parameters	Group I (%)	Group II (%)	p-value	Name of Test
Oligohydramnios	12 (30)	2 (5)	0.01	Fisher exact test
Abruption placenta	5 (12.5)	0	0.01	Fisher exact test
Eclampsia	7 (17.5)	0	0.01	Fisher exact test
C-Section	18 (45)	8 (20)	0.001	Chi-square test
Maternal Mortality	2 (5)	0	0.619	Fisher exact test

C-Section: Caesarean-Section

the levels of serum Vitamin D and serum calcium decrease the diastolic and systolic blood pressure increase (Table 3).

Mean gestational age of patients in Group I was 36.34±2.64 weeks and in Group II 38.26±1.64 weeks giving p=0.001 which was highly significant. Mean birth weight of newborn in Group I patients was 2150.24±314.82 grams and 2787.60±233.15 g in Group II patients giving p=0.001 which was highly significant. In Group I, 12.5% newborn developed acute respiratory distress syndrome, and no newborn of Group II developed acute respiratory distress syndrome giving p=0.001 which was highly significant. In Group I, 22.5% newborns had got APGAR <7 at 5 min as compared to 2.5% of patients of Group II giving p=0.001. 32.5% newborns of Group I were admitted to NICU (neonatal intensive care unit) as compared to 2.5% of patients of Group II who were admitted to NICU giving p=0.001 which was highly significant. 27.5% fetus of Group I patients have fetal growth restriction as compare to 5% of fetus of Group II giving p=0.001 which was highly significant. About 5% of babies of Group I has got perinatal mortality as compare to Zero in Group II patients giving p=0.01 which was significant (Table 4).

In Group I, 30% of patients developed oligohydramnios as compared to 5% of patients of Group II giving p=0.01 which was significant. About 12.5% of patients of group I had got abruption placenta and Zero patients of Group II developed abruption giving p=0.01 which was significant. About 17.5% of patients of Group I developed eclampsia as compared to zero patients of Group II giving p=0.01. 45% of patients in Group I had undergone C-section as compare to 20% of patients in Group II giving p=0.001 which was highly significant. In Group I, there was 5% maternal mortality as compared to 0% in Group II giving p=0.619 (Table 5).

DISCUSSION

The maternal and perinatal outcome of patients and levels of serum calcium and serum Vitamin D was evaluated in patients of pregnancy-induced hypertension and normal antenatal patients. The levels of serum Vitamin D and calcium were found significantly lower in patients with pregnancy-induced hypertension than in normal pregnant patients.

In our study the mean age of patients in Group I was 23.23±1.78 years and in Group II 26.50±1.30 years giving a p=0.696 which was non-significant which was in accordance to study done by Dalmar et al. [7] which also showed no difference in age distribution in two groups. The mean systolic blood pressure in group I was 158.60±6.49 mm Hg and in

Group II it was 119.60± 3.28 mm Hg with the p=0.003 which was highly significant which was in accordance to a study done by Dhillon et al. [8] where mean systolic blood pressure in Group I was 156.50±4.6 mm Hg and 114.5±4.6 mm Hg in Group II. The mean diastolic blood pressure in group I was 110.00±5.11 mm Hg and 79.50±2.66 mm Hg in Group II with p=0.003, which was highly significant. It was in accordance to a study done by Aghade et al. [5] which also showed significantly higher mean diastolic blood pressure of 120.53±7.54 mm Hg in Group I patients as compare to 74.8±5.2 mm Hg in Group II.

The mean serum Vitamin D levels were 22.30±6.11 ng/ml in Group I and the mean serum Vitamin D level was 36.68±9.34 ng/ml in Group II giving p=0.016 which was in accordance to study done by Singla et al. [9], which also showed significantly lower levels of serum Vitamin D (19.3±4.3 ng/ml) in patients with pregnancy-induced hypertension as compared to 34.42 ±5.2 ng/ml in normal antenatal patients. The mean serum calcium levels in Group I were 8.58±0.63 mg dl and 9.27±0.40 mg/dl in Group II giving a p=0.018 which was highly significant. It was in accordance to a study done by Lavyakumari et al. [10] which also showed levels of serum calcium in patients with pregnancy-induced hypertension was 8.17±0.15 mg/dl as compare to 9.12±0.34 mg/dl in normal pregnancy.

The mean gestational age in Group I was 36.34±2.64 weeks and 38.26±1.6 weeks in Group II giving p=0.001 which was highly significant it was in accordance to a study done by Verma et al. [11] which also showed the fetus in pregnancy-induced hypertension patients required delivery at an early gestational age of 35.3±1.43 weeks. The mean birth weight in Group I was 2150.24±314.82 gms and 2787.60±233.15 gms in Group II with p=0.001 which was highly significant. It was in accordance to a study done by Kumar et al. [12] which showed patients with pregnancy-induced hypertension had a low mean birth weight of 2177±0.282 gms. In group I, 12.5%of babies developed ARDS as compare to 0 in Group II giving p=0.001 which was in accordance to a study done by Deshpande et al. [13] which showed 14% of babies of pregnancy-induced hypertension developed ARDS as compared to 1% in normal antenatal patients. Perinatal mortality was 5% in Group I and 0 in Group II giving p=0.01, study done by Sahu et al. [14] also showed perinatal mortality of 4% in patients with pregnancy-induced hypertension as compare to 0.5% in normal antenatal patients. About 30% of patients of Group I and 5% of patients of Group II developed oligohydramnios giving p=0.01 which was in accordance to a study done by Pairu et al. [15] which showed 28% of patients with pregnancy-induced hypertension developed oligohydramnios as compare to 4% of patients in normal antenatal patients. About 45% of patients in Group I and 20% of patients in Group II undergo C-section giving p=0.001 which was highly significant. It was in accordance to a study done by Jindal et al. [16] which showed 37% of patients undergo C-section in pregnancy-induced hypertension as compared to 15% in normal antenatal patients. Maternal mortality was 5% in Group I and 0 in Group II with p=0.619, it was in accordance with study done by Roy et al. [17] which showed maternal mortality was 3.8% in patients with pregnancy-induced hypertension.

Limitation
Due to small sample size the result cannot be generalized.

CONCLUSION

Serum levels of 25 (OH) Vitamin D and calcium have a significant relationship with pregnancy-induced hypertension. Low levels of calcium and 25 (OH) Vitamin D cause increased risk of pregnancy-induced hypertension and supplementation of these reduces the incidence of pregnancy-induced hypertension. Hence, their supplementation can be used as a possible intervention strategy in preventing one of the most common causes of perinatal and maternal morbidity and mortality around the world.

FUNDING

Nil.

CONFLICTS OF INTEREST

Nil.

ETHICAL COMMITTEE APPROVAL

Yes.

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