European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 9, Issue 3, Winter 2022

ORIGINAL RESEARCH

Role Of Serum Calcium As A Predictive Factor In Pregnancy Induced Hypertension

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ABSTRACT

Aim: To compare serum calcium status in pregnant women with and without PIH.
Material and method:It was a hospital based prospective observational study conducted in the department of Obstetric and Gynecology, National Capital Region Institute of Medical Sciences, Meerut for a period of 12 months. 200 antenatal cases after 20 weeks pregnancy having age between 18-40 years were divided into 2 types based on BP i.e. Cases-100 patients of PIH (Pregnancy induced hypertension) and Control- 100 normotensive patients. A detailed family and medical history of all the childbearing women with gestational age 20 weeks or more admitted with the features of HDP (hypertension disorder of pregnancy) was recorded followed by a thorough clinical examination. Systolic and diastolic blood pressure of all the participants was carefully recorded every four hourly. Serum calcium levels were measured by the O- Cresol PhthaleinComplexone (OCPC) method.
Results: Mean SBP in case and control group was 152.30±10.45 and 118.20±7.66 respectively. Mean DBP in case and control group was 99.42±7.29 and 75.82±5.21 respectively. Hence SBP and DBP was higher in case group as compared to control group. According to Pearson correlation analysis, negative significant correlation was found between BP and serum calcium(mg/dL) i.e. with increase in BP, there is decrease in serum calcium(mg/dL).
Conclusion:The present study emphasizes the need of monitoring serumcalcium during antenatal period and appropriatemeasures may reduce the incidence of PIH.In areas where dietary calcium intake is low,calcium supplementation during pregnancy (atdoses of 1.5–2.0 g elemental calcium/day) isrecommended for the prevention of PIH in all women, but especially those athigh risk of developing PIH.
Keywords: PIH, Calcium, BP

INTRODUCTION

Hypertension during pregnancy with or without proteinuria is one of the leading causes of maternal and perinatal morbidity and mortality all over the world[1-2], accounting for more than 40,000 maternal deaths annually[3]. Pregnancy induced hypertension (PIH) is defined as systolic blood pressure (SBP) >140mmhg and diastolic blood pressure>90mmhg. The

incidence of PIH in India is 7-10% of all pregnant women[4]. PIH refers to one of four conditions:

a) Pre-existing hypertension
b) Gestational hypertension and pre-eclampsia
c) Pre-existing hypertension plus superimposed Gestational hypertension with proteinuria
d) Unclassifiable hypertension[5]

When pre-eclampsia is associated with seizures it is defined as eclampsia[4].According to latest guidelines of ACOG, Preeclampsia is a multisystem progressive disorder characterized by the new onset of hypertension and proteinuria or the new onset of hypertension and significant end-organ dysfunction with or without proteinuria in the last half of pregnancy or postpartum. It is associated with various complications like disturbed autoregulation of cerebral circulation, visual disturbances, oliguria, pulmonary edema, and fetal growth restriction[6]. The hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome, a serious manifestation of preeclampsia, contributes to increased morbidity and mortality in this disorder. If untreated, preeclampsia progresses to eclampsia manifesting as convulsions, which may lead to confusion, coma, and death[7].

The etiology of PIH is unknown despite decades of intensive research worldwide. This is a disorder of hypothesis and affliction to involve all organs in the body. A number of dietary deficiencies or excesses have been blamed as the cause of PIH over centuries one of them being calcium deficiency. During pregnancy there is great demand for calcium intake to respond to higher demands for calcium caused by the process of fetal bone formation[8].

Calcium supplementation during pregnancy is known to decrease incidence as well as severity of gestational hypertension, pre-eclampsia, eclampsia and also neonatal morbidity and mortality, as well as pre-term births, especially in developing countries[9-11], although the impact varies according to the baseline calcium intake and other prevailing risk factors in the population[12,13]. The underlying mechanism can be explained by reduction in parathyroid calcium release and intracellular calcium concentration, in woman taking calcium supplementation during pregnancy, thereby reducing smooth muscle contractility and promoting vasodilatation and hence, decreasing the risk and or severity of HDP[14,215]. Calcium also increases magnesium levels causing indirect effect on smooth muscle function[16].

In developing countries, nutritional deficiency of essential trace elements is a common health problem, particularly among pregnant women because of increased requirements of various nutrients. Accordingly, this study was initiated to compare serum calcium status in pregnant women with and without PIH.

MATERIAL AND METHODS

It was a hospital based prospective observational study conducted in the department of Obstetric and Gynecology, National Capital Region Institute of Medical Sciences, Meerut for a period of 12 months. 200 antenatal cases after 20 weeks pregnancy having age between 18-40 years were divided into 2 types based on BP:

Cases-100 patients of PIH (Pregnancy induced hypertension)

Control- 100 normotensive patients)

The sample size was recruited according to the following inclusion and exclusion criteria.

INCLUSION CRITERIA

STUDY GROUPS

CASES

1. Diagnosed PIH based on criterias: BP≥140/90mmHg on 2 separate occasions 6 hrs apart, Proteinuria more than 300mg in 24 hrs urine or 1+ dipstick in 2 midstream urine samples collected 4 hrs apart.

2. More than 20 weeks gestation
3. Singleton pregnancy
4. Age 18-40 yrs
5. Non diabetic

CONTROL GROUPS

1. BP < 140/90mmHg
2. More than 20 weeks gestational age
3. Singleton pregnancy
4. Age 18-40 yrs
5. Non diabetic

EXCLUSION CRITERIA

1. Chronic HTN
2. Gestational Diabetes Mellitus
3. Renal disease, cardiac,pulmonary disease
4. Age<18yrs and >40yrs
5. Non anemic
6. Multiple pregnancy

DATA COLLECTION

1. History taking: Age, menstrual history, obstetrical history, personal history, medical, surgical, and family history.
2. Physical Examination- General and Systemic
3. Fundus examination
4. Obstetric examination- P/A, P/S, P/V
5. Investigations: CBC, ABORh, Blood sugar, HIV, HCV, HBsAg, VDRL, LFT, KFT, Serum calcium, Serum TSH, Urine R/M, Coagulation Profile, PT INR, USG, ECG.

A detailed family and medical history of all the childbearing women with gestational age 20 weeks or more admitted with the features of HDP was recorded followed by a thorough clinical examination. Systolic and diastolic blood pressure of all the participants was carefully recorded every four hourly.

Urine analysis was done in all subjects to measure the degree of proteinuria and to differentiate patients with gestational hypertension from preeclampsia. The degree of proteinuria was measured by dipstick and graded as Trace to 4+ (Trace, 0.1gm/L;1+, 0.3gm/L;2+, 1gm/L;3+, 3.0gm/L;4+, 10gm/L). At the same time blood was taken from the ante-cubital vein using a sterile needle and syringe early in the morning after overnight fasting for serum calcium measurement. Blood samples were allowed to clot and then centrifuged at 3000 revolutions per minute for 10 minutes. Serum calcium levels were measured by the O- Cresol PhthaleinComplexone (OCPC) method.

Data was collected and subjected to statistical analysis.

STATISTICAL ANALYSIS

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). For each assessment point, data were statistically analyzed using one way ANOVA. Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.

RESULTS

Maximum patients were from the age group of 21-25 years followed by 25-30 years. Only 9 subjects were from the age group of >30-35 years. Hence the age was comparable among the groups. Gestational age viz. <37 and >37 weeks was revealed in 48%, 52% and 34%, 66% of the subjects in case and control group respectively with statistically significant difference as $p<0.05$. Past history of PIH was found in 4% and 1% of the subjects in case and control group respectively with statistically insignificant difference as $p>0.05$ (table 1).

Table 1: Age, gestational age(wks), gravidity, family history, past history distribution among the study subjects

Group	**Age Group (in years)**				**p value**
	21-25	**>25-30**	**>30-35**		
Case	54	42	4		0.82
Control	58	37	5		
Group	**Gestational Age (wks)**				
	<37	**>37**			
Case	48	52			0.044
Control	34	66			
Gravidity	**Case (PIH)**		**Control**		**p value**
	N=100	**%**	**N=100**	**%**	
Primigravida	36	36	37	37	0.94
Multigravida	64	64	63	63	
History	**Case (PIH)**		**Control**		**p value**
	N=100	**%**	**N=100**	**%**	
Yes	6	6	2	2	0.63
No	94	94	98	98	
Past History	**Case (PIH)**		**Control**		**p value**
	N=100	**%**	**N=100**	**%**	
Yes	4	4	1	1	0.76
No	96	96	99	99	

Mean BMI was comparatively higher in case group (25.57) as compared to control group (23.91), though statistically no significant difference was found. Mean SBP in case and control group was 152.30±10.45 and 118.20±7.66 respectively. Mean DBP in case and control group was 99.42±7.29 and 75.82±5.21 respectively. Hence SBP and DBP was higher in case group as compared to control group. When mean SBP, DBP was compared statistically using t test between case and control group, it was found to be highly significant difference as $p<0.05$ (table 2).

Table 2: BMI (kg/m^2), BP among the study subjects

Group	**BMI (kg/m^2)**		**t test**	**p value**
	Mean	**SD**		
Case (PIH)	25.57	5.78	1.69	0.23
Control	23.91	4.81		
	Systolic BP (mmhg)		**t test**	**p value**
	Mean	**SD**		
Case (PIH)	152.30	10.45	27.56	<0.01*
Control	118.20	7.66		
	Diastolic BP (mmhg)		**t test**	**p value**
	Mean	**SD**		
Case (PIH)	99.42	7.29	26.83	<0.01*

Control	75.82	5.21		

*: statistically significant

Mean serum calcium(mg/dL) in case and control group was 8.33±1.01 and 9.59±0.84 respectively. Hence serum calcium (mg/dL) was higher in control group as compared to case group with highly significant difference as p<0.05 (table 3).

Table 3: Serum calcium(mg/dL) among the study subjects

Group	Serum calcium (mg/dL)		t test	p value
	Mean	SD		
Case (PIH)	8.33	1.01	19.52	<0.01*
Control	9.59	0.84		

Table 4: Correlation between serum calcium(mg/dL) and blood pressure

Parameters	Serum calcium (mg/dL)	
	r value	p value
SBP	-0.33	0.003
DBP	-0.30	0.006

*: statistically significant

According to Pearson correlation analysis, negative significant correlation was found between BP and serum calcium(mg/dL) i.e. with increase in BP, there is decrease in serum calcium(mg/dL) as shown in table 4.

DISCUSSION

Changes in intracellular calcium concentrations seem to be involved in the pathogenesis of pregnancy induced hypertension[8].

The mean age in case and control group was 25.7±5.07 and 25.6±4.82 years respectively. Maximum patients were from the age group of 21-25 years followed by 25-30 years. Only 9 subjects were from the age group of >30-35 years. Hence the age was comparable among the groups in our study. Similar age distribution was reported by S Priyankaet al[8] andNaina Kumar et al[17] in their studies. Contrary to this Lamminppaet al[18] mentioned higher incidence of pre eclampsia in advanced maternal age.

In both the group, maximum women have multiple gravidity in this study.S Priyankaet al[8] in their study showed that the mean gestational age among study population was (31.5±2.72 weeks) among PIH cases and (31.6±3.32 weeks) among normal controls and in PIH cases majority of PIH cases (75%) are above 30 weeks of gestation. This is similar to the study done by Ebeigbe PN et al[19] where 91.3% of patients of PIH were of gestational age more than 24 weeks. A study by Hanmantha VW[20] showed a mean gestational age of (38.42±4.16 weeks) which is slightly higher than the present study.

Mean BMI was comparatively higher in case group (25.57) as compared to control group (23.91), though statistically no significant difference was found in this study. Ephraim et al[21] in their study too found no significant difference w.r.t. BMI among the case and control group.

Mean SBP in case and control group was 152.30±10.45 and 118.20±7.66 respectively. Hence SBP was higher in case group as compared to control group. When mean SBP was compared statistically using t test between case and control group, it was found to be highly significant difference as p<0.05. Mean DBP in case and control group was 99.42±7.29 and 75.82±5.21 respectively. Hence DBP was higher in case group as compared to control group. S Priyanka et al[8] in their found that the mean Systolic Blood Pressure (SBP) among PIH cases was 147.65±3.74 mm of Hg and 102.5±2.01 mm of Hg among control subjects and the mean Diastolic Blood Pressure (DBP) among PIH cases was 109.5±3.89mm of Hg and among

controls was 71.75±3.059 mm of Hg which are both statistically significant. ($p<0.0001$).Study by Naser M.O et al[22] from Saudi showed a mean SBP of 171.20±20.88 mmhg among controls whereas a mean SBP of 111.20±6.39 mm of Hg among controls and a mean DBP of 104.80±10.84 mm of Hg and 75.33±5.16 mm of Hg among cases and controls respectively whose values are higher than the present study. In a study conducted by Mulkhed S.V et al[23] showed a mean SBP of 170.68±13.34 mm of Hg in PIH cases and a mean SBP of 129.28±8.01 mm of Hg among control subjects which is higher than the present study.

Mean serum calcium (mg/dL) in case and control group was 8.33±1.01 and 9.59±0.84 respectively. Hence serum calcium (mg/dL) was higher in control group as compared to case group. According to Pearson correlation analysis, negative significant correlation was found between BP and serum calcium (mg/dL) i.e. with increase in BP, there is decrease in serum calcium (mg/dL) in our study.The reason for decreased serum calcium levels in the present study may be due to decreased intake, or decreased absorption orlosses from the body. Moreover, it was proposed that the beneficial effects of calcium supplementation in the prevention of PIH could be related with the maintenance of the plasma ionized calcium levels within the narrow physiologic change. The concentration of extracellular ionized calcium is crucial for the synthesis in the endothelium of vasoactive substances, such as prostacyclin and nitric oxide.

Similarly S Priyankaet al[8] in their study showed that the mean serum calcium levels in the PIH group was 8.47±0.208 mg/dl, while the serum calcium of the control group was 9.423±0.157mg/dl. There was statistically significant difference in both groups ($p=0.0001$).Naina Kumar et al[17] in their study found that the mean±SD levels of serum calcium in women with gestational hypertension, pre-eclampsia and eclampsia were 8.83±0.55, 8.55±0.89 and 8.41±0.76 mg/dl respectively, indicating that maternal hypocalcaemia was associated with more severe disease. These findings are similar to our study.

Another study by Punthumapol C et al[15] also reported that the maternal serum calcium levels were significantly lower in women with severe pre-eclampsia (8.7 +/- 0.59 mg/dl vs. 8.99 +/- 0.31 mg/dl, $p = 0.045$; and 9.05 +/- 0.52 mg/dl, $p = 0.014$) as compared to normal pregnant women and those with mild pre-eclampsia.

On contrary, studies by S.Golmohammedlouet al[24], Villanueva LA et al[25] and Richards SRet al[26] found no difference in serum calcium levels among PIH cases and control subjects. This may be due to the inclusion of small study populations in these studies.

The present study was conducted on a small group of childbearing women with hypertensive disorder of pregnancy. Dietary patterns were not determined, thus the impact of inadequate intake of this mineral as well as possible confounding effect of diet remains.

CONCLUSION

The findings of the present study demonstrate lower levels of serum total Ca in pre-eclampsia compared to normal pregnancy. Serum total Ca level was found decreasing with the severity of PIH. Thus, these trace elements alongwith other serum biomarkers would definitely be helpful ineffective management of PIH.Therefore, this study may alert Obstetrician andpatients to the harmful effect of this dietary deficiency on Pregnancy outcome. It also emphasizes the need of monitoring serumcalcium during antenatal period and appropriatemeasures may reduce the incidence of PIH.In areas where dietary calcium intake is low,calcium supplementation during pregnancy (atdoses of 1.5–2.0 g elemental calcium/day) isrecommended for the prevention of PIH in all women, but especially those athigh risk of developing PIH.

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