

# The study of serum calcium in pregnancy induced hypertension and normal pregnancy and its correlation with pregnancy induced hypertension

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## Abstract

**Background:** Pregnancy induced hypertension is a type of high risk pregnancy which complicates 7-10% of all pregnant women. Changes in intracellular calcium concentrations seem to be involved in the pathogenesis of pregnancy induced hypertension. **Methods:** The present study was undertaken in 80 pregnant women. Data for the study was collected from 40 normo tensive pregnant women with more than 20weeks of gestational age (control group) and 40 pregnancy induced hypertensive patients (study group) attending for antenatal care in Department of Obstetrics and Gynaecology in government maternity hospital (of tertiary teaching hospital). Cases and controls were matched. Serum calcium levels were estimated by spectrophotometry method. **Results:** The mean serum calcium is significantly lower in PIH group (8.47± 0.208mg/dl) compared to normal pregnancy (9.423± 0.157mg/dl). There was statistically significant difference in both groups (p=0.0001). **Conclusion:** The serum calcium levels are decreased in PIH patients compared to normotensive pregnant women, suggesting the possible role of calcium in etiopathophysiology of PIH.

**Key Words:** Pregnancy induced hypertension, normal pregnancy, serum calcium, blood pressure.

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## INTRODUCTION

Hypertensive disorders in pregnancy complicate 1 in 10 pregnancies, often associated with maternal and neonatal mortality and morbidity (jain, 1997). Pregnancy induced hypertension is a hypertensive disorder in pregnancy that occurs after 20 weeks of pregnancy in the absence of other causes of elevated blood pressure (bp) (>140/90mm hg). When PIH is associated with proteinuria (protein in urine > 0.3gm/24 hours) it is termed as pre-eclampsia. When pre-eclampsia is

associated with seizures it is defined as eclampsia<sup>1</sup>. The incidence of PIH in India is 7-10% of all pregnant women. 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. There are various etiological factors for PIH like Abnormal placentation (steegers *et al.*, 2010), vasculopathy and inflammatory changes, immunological factors, genetic factors, nutritional factors (amir *et al.*, 1998). 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. Furthermore there is a dilution of cation due to expanded cellular fluid volume, and to normal hypercalciuria of pregnancy consequent to increased glomerular filtration. Thus serum ionized calcium concentrations depend on an adequate calcium intake. On the basis of experimental findings no precise mechanism has been established relating serum calcium levels with PIH. One of the possibility is that PIH women have a

significantly lower 1, 25-dihydroxy vitamin D. This lower level may contribute to the suboptimal intestinal absorption of calcium during the time of increased calcium demand (aemer imdad *et al.*,2011). Further, low calcium intake results in high parathyroid hormone levels and increased membrane permeability, resulting in increased intracellular calcium levels and decreased serum calcium levels. The former triggers vascular smooth muscle contraction and contributes to increased blood pressure (seely *et al.*,1992). 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.

**MATERIALS AND METHODS**

The present study was conducted at Govt. Maternity Hospital, Hanamkonda, Kakatiya Medical College, Warangal. This study is a case control study done in the Department of Physiology and Dept. of Obstetrics and Gynaecology, Kakatiya Medical College, Warangal.

**Inclusion Criteria**

Diagnosed PIH based on criteria BP  $\geq$ 140/90 on two separate occasions 6 hrs apart, proteinuria more than 300mg in 24 hr urine. Singleton pregnancy. Age 15-40 years. More than 20 weeks gestation age. Non-diabetic.

**Exclusion Criteria**

Chronic Hypertensives. Gestational Diabetes Mellitus. Renal Disease

**Methods**

Ethics approval for the study was obtained from the hospital/institutional Ethical Committee. Written information about the study was supplied to hospital. Pregnant women presenting with PIH were included in the case group, and pregnant women who were admitted for normal institutional delivery were included in control group. Written consent about including the subjects/patients into the study was taken from patients and attendants.

**RESULTS**

All the values were expressed as mean  $\pm$  SD (Standard Deviation). p value  $<$ 0.05 was considered as statistically significant, that  $<$ , =0.001 was considered as highly significant Pearson’s correlation coefficient (r) was calculated to assess the correlation between biochemical parameters and the blood pressure.

**Table 1:** Comparative statistics: of age, gestational age, Systolic BP, Diastolic BP in controlled and PIH groups (SD- Standard deviation)

Characteristics	Groups	Mean $\pm$ SD	T	p
Age(20-40yrs)	PIH Cases	25.4 $\pm$ 5.44		
	Control	24.9 $\pm$ 4.72	0.46	0.323
Gestational age(wks)	PIH Cases	31.5 $\pm$ 2.72		
	Control	31.6 $\pm$ 3.32	0.184	0.85
Systolic BP(mm of Hg)	PIH Cases	147.65 $\pm$ 3.74		
	Controlled	109.5 $\pm$ 3.89	14.26	0.0001
Diastolic BP(mm of hg)	PIH Cases	102.5 $\pm$ 2.01		
	Controlled	71.75 $\pm$ 3.059	16.96	0.0001

[Table 1] shows comparative statistics of controlled and PIH groups as follows

1. Mean age in years and Mean gestational period in weeks and were not statistically different in controlled and PIH groups.
2. Systolic and diastolic blood pressures were highly significantly higher in PIH group than controlled group.

**Demographic data**

**Table 2:** Distribution of total study population

Group	No of Cases	percentage
Normal pregnant women	40	50%
Pregnant women with PIH	40	50%
<b>Total</b>	<b>80</b>	<b>100%</b>

[Table No.2]. shows distribution of total study subjects of whom 50% are pregnant women with PIH are cases and remaining 50% of normal pregnant women are controls.

**Table 3:** Biochemical parameters

Parameter	Cases(n=40)	Controls(n=40)	p-value	Significance
Serum calcium (mg/dL)	8.47 $\pm$ 0.208	9.423 $\pm$ 0.157	0.000	Highly significant

The mean serum total calcium was decreased in the present study. The mean serum calcium levels in the PIH group was 8.47 $\pm$ 0.208 mg/dl, while the serum calcium of the control group was 9.423 $\pm$ 0.157mg/dl. There was statistically significant difference In both groups (p=0.0001). When serum calcium, levels were correlated independently with systolic and diastolic blood pressure, a significant negative correlation was obtained.

**Table 4:** Correlation of severity

Parameter	Systolic Blood Pressure	Diastolic Blood Pressure
Serum calcium	r= -0.121; p= 0.0001	r= -0.0038; p= 0.0001

Where r - Karl Pearson correlation Co-efficient (-1 to +1), p $<$ 0.05= statistically significant; p $<$ 0.001= highly significant.

**DISCUSSION**

PIH is a type of high risk pregnancy which complicates 7-10% of all pregnant women. PIH occurs after 20 weeks of pregnancy in the absence of other causes of elevated blood pressure (BP) ( $\geq$ 140/90 mm of Hg measured 2

times with at least of 6 hr interval) When PIH is associated with significant proteinuria (protein in urine  $\geq 0.3$  g/in 24 h) it is termed as Pre-Eclampsia. When Pre-Eclampsia is associated with seizures, it is defined as Eclampsia<sup>1</sup>. Changes in intracellular calcium concentrations seem to be involved in the pathogenesis of pregnancy induced hypertension<sup>2</sup>. The present study is a case control study done in a tertiary care teaching hospital, to compare total serum calcium levels in PIH cases and normal pregnant women as controls of matched age group after careful thorough examination. Total study population includes 80 pregnant women of which 40 pregnant women with hypertension, edema, proteinuria were taken as cases (50%) and 40 normal pregnant women taken as controls (50%) (Table 2). In the present study of the 80 study population about 48 women (60%) belongs to age group less than 25 years and 32 (40%) pregnant women were above 25 years age. This is similar to the study done by Ebeigbe PN *et al.*<sup>3</sup>. Akther *et al.*<sup>4</sup>, Amandeep kaur *et al.*<sup>5</sup>. Sudarsan S *et al.*<sup>6</sup> who concluded that eclampsia involves young primigravidas and 87.60% of eclampsia patients were less than 25 years of age in their study.(Table 1). In contrast to present study Bangal VB *et al.* (2011)<sup>7</sup> reported majority of pregnant women were in age group of less than 20 years of age. The mean age of presentation in the present study is (25.4 $\pm$ 5.44yrs) among PIH cases and (24.9  $\pm$  4.72yrs) among normal controls. Similar findings have been observed by Vinodhini and kumari *et al.* (24-29yrs)<sup>8</sup>, and Meshram *et al.*, (mean age of patients with PIH 24.55yrs)<sup>6</sup>. Study by Bangal. VB *et al.*<sup>7</sup> found the incidence of PIH was higher among teenage pregnancy. Duckitt *et al.*<sup>9</sup> observed teenage pregnancy to be one of the risk factors for PIH and eclampsia. Contrary to this Lamminppa *et al.*<sup>10</sup> mentioned higher incidence of pre eclampsia in advanced maternal age. Jasovic Siveska *et al.*<sup>11</sup> mentioned bi modal variability i.e, PIH among young primipara and old multipara females. In the present study the mean gestational age among study population was (31.5 $\pm$ 2.72 weeks) among PIH cases and (31.6 $\pm$ 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.*<sup>3</sup> where 91.3% of patients of PIH were of gestational age more than 24 weeks. A study by Hanmantha VW (2012)<sup>12</sup> showed a mean gestational age of (38.42 $\pm$ 4.16 weeks) which is slightly higher than the present study (Table 1). In the present study among 80 total study population 51 pregnant women (63.75%) are primigravida and 29 pregnant women (36.25%) of pregnant women are 2<sup>nd</sup> gravida or multigravida. Of the 40 PIH cases 30 cases (75%) are primi gravida and remaining 10 (25%) are 2<sup>nd</sup> gravida or multi gravida. These findings are in line with

Hanmantha *et al.*<sup>12</sup>, in which 67.33% of cases with PIH were primigravida and 16.34% were of 2<sup>nd</sup> gravida while 16.34% were of 3<sup>rd</sup> and above gravida pregnant women. This was also agreed by Bangal VB *et al.*<sup>7</sup>, Bhattacharya SM *et al.*<sup>13</sup>, in which 65% and 65.5% of PIH cases respectively were primigravida. Duckitt *et al.*<sup>9</sup>, Jose villar *et al.*<sup>14</sup> also reported that primigravida was a risk factor for pre eclampsia and eclampsia, thus once again proving the fact that PIH is most common in first pregnancy. In a study from Ethiopia 66.7% of cases with PIH studied by Wolde *et al.*<sup>15</sup> were nulliparous and study by Riaz *et al.*<sup>16</sup> showed 60% of the cases were primigravida. The mean Systolic Blood Pressure (SBP) in the present study among PIH cases was 147.65 $\pm$ 3.74 mm of Hg and 102.5 $\pm$ 2.01 mm of Hg among control subjects and the mean Diastolic Blood Pressure (DBP) among PIH cases was 109.5 $\pm$ 3.89mm of Hg and among controls was 71.75 $\pm$ 3.059 mm of Hg which are both statistically significant. (p<0.0001) (Table 1). Study by Naser M.O *et al.*<sup>17</sup> from Saudi showed a mean SBP of 171.20 $\pm$ 20.88 mm of Hg where as a mean SBP of 111.20 $\pm$ 6.39 mm of Hg among controls and a mean DBP of 104.80 $\pm$ 10.84 mm of Hg and 75.33 $\pm$ 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, Irani F.B *et al.*<sup>18</sup> showed a mean SBP of 170.68 $\pm$ 13.34 mm of Hg in PIH cases and a mean SBP of 129.28 $\pm$ 8.01 mm of Hg among control subjects which is higher than the present study. The mean serum total calcium was decreased in the present study. The mean serum calcium levels in the PIH group was 8.47 $\pm$ 0.208 mg/dl, while the serum calcium of the control group was 9.423 $\pm$ 0.157mg/dl. There was statistically significant difference in both groups (p=0.0001). This result matches previous data which suggest that an inverse relationship between calcium and incidence of PIH (Table 3). The serum calcium level results of the present study are in agreement with that of Aruna Patel *et al.* (2010)<sup>19</sup>, Sharma, Dinesh Kumar *et al.* (2014)<sup>20</sup>, Akhter *et al.* (2010)<sup>4</sup>, Malas NO, Shurideh ZM *et al.*(2000)<sup>17</sup>, A H Mohieldien *et al.*(2007)<sup>21</sup>, Sabitha Bai T, Rudrappa G *et al.* (2014)<sup>22</sup>, Idogun ES, Imarengiaye CO *et al.*(2007)<sup>23</sup>, Punthumapol C, Kittichotpanich B *et al.* (2007)<sup>24</sup>, Amandeep Kaur *et al.*<sup>5</sup>, Sukonpan K, Phupong V *et al.*(2005)<sup>25</sup>, Farzin L, Sajadi F *et al.* (2011)<sup>26</sup>, Rathi B, Tadas A *et al.* (2014)<sup>27</sup>, Jagannath Pairu, Triveni GS, Ankitha Manohar *et al.*<sup>28</sup>, Sakina Roohi, Jiyauddin *et al.*(2008)<sup>29</sup>, Guhan VN, Jeyakumar M, K Prabhakar Rao *et al.*(2013)<sup>30</sup>, Dilutpal Sharma, Depapriya Bandyopadhyay *et al.*<sup>31</sup>, whose studies showed a decreased mean serum calcium levels in PIH cases when compared to the control subjects. The reason for decreased serum calcium levels in the present study may be due to decreased intake, or decreased absorption or

losses 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 (Seely *et al* 1992). The concentration of extracellular ionized calcium is crucial for the synthesis in the endothelium of vaso active substances, such as prostacyclin and nitric oxide (Lopez *et al* 1987) On contrary, studies by S.Golmohammedlou *et al* (2008)<sup>32</sup>, Villanueva LA, Figueroa A *et al.*,(2001)<sup>33</sup> and Richards SR, Nelson DM *et al.*,(1984)<sup>34</sup> 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. In the present study significant negative correlation of serum calcium with systolic blood pressure and diastolic blood pressure in PIH pregnant women suggests strong relationship between deficiency of calcium element and risk of PIH (Table 4).

### LIMITATIONS

The present study was done at a referral center; hence it could not be extrapolated to general population trend. Dietary patterns were not determined, thus the impact of inadequate intake of this mineral as well as possible confounding effect of diet remains. Findings from the study remains relevant and add to evidence on the subject matter. However with the present study findings it is strongly recommended that further larger studies are required and other measures of serum calcium estimation should be undertaken to confirm the findings in the present study.

### CONCLUSIONS

From this study it may be concluded that

- Serum calcium levels in Pregnancy Induced Hypertension females were found to be lower than the values observed in case of normal pregnant females.
- Decrease in serum calcium in PIH pregnant females could be due to either decreased intake or defective intestinal absorption or decreased renal tubular reabsorption.
- It may be concluded that deficiency of calcium in Pregnancy Induced Hypertension women may be related to their inadequate dietary intake and this macronutrient deficiency may be a risk factor for development of high blood pressure and Pregnancy Induced Hypertension.

### RECOMMENDATIONS

- Information, education and communication (IEC) strategies should be strengthened to increase the

enrollment of women for regular antenatal check-up particularly mothers having preexisting high risk factors of PIH.

- Focus on strengthening of quality of antenatal services for early diagnosis of PIH like blood pressure, urine albumin as early recognition and prompt treatment reduces the complications.
- Need of more community based research specifically in the area of preventive management of PIH cases so has to minimize complications.
- Therefore, this study may alert Obstetrician and patients to the harmful effect of this dietary deficiency on Pregnancy out come. It also emphasizes the need of monitoring serum calcium during antenatal period and appropriate measures may reduce the incidence of preeclampsia.
- In areas where dietary calcium intake is low, calcium supplementation during pregnancy (at doses of 1.5–2.0 g elemental calcium/day) is recommended for the prevention of pre-eclampsia in all women, but especially those at high risk of developing pre-eclampsia.[W.H.O]<sup>35</sup>.

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