

1 Study of Serum and Urinary Calcium Levels in Pregnancy 2 Induced Hypertension Cases in and Around Chitradurga

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7 **Abstract**

8 Pregnancy Induced Hypertension (PIH) is defined as multisystem disorder of unknown
9 aetiology causing vasospasm and anoxia and there is a raised blood pressure recorded at least
10 on two occasions at 6 hours apart. It is thought that preeclampsia develop when the pregnancy
11 induced systemic response causes one or more maternal system to decompensate. The high
12 foetal demand for calcium is facilitated by profound physiological interactions between mother
13 and foetus. Biochemical changes in PIH are increased plasma Creatinine, urea and uric acid
14 concentration with proteinuria due to renal glomerular endotheliosis leading to impaired
15 glomerular perfusion and filtration. A case control comparative study was done with PIH and
16 normal pregnant women both from outpatient and inpatient of Basaveshwara Medical College
17 Hospital and Research Centre, Chitradurga, according to the criteria. Study group will be
18 followed up every four weeks from 28th week of gestation and 24hour/random urine sample
19 will be collected for Biochemical evaluation of urinary Calcium, Creatinine and protein.

21 **Index terms**— PIH, Urinary calcium, Creatinine, Protein and Protein/Creatinine ratio, serum uric acid.

22 **1 Introduction**

23 Hypertension is one of the common complications met with pregnancy and contributes significantly to maternal and
24 perinatal morbidity and mortality. There is generalised vasospasm leading to systemic disorders involving all the
25 vital organs of the body. Severity of Hypertensive disease in pregnancy is controllable with proper management
26 in most of the cases and mortality is avoidable. PIH is a term used to describe new hypertension which appear
27 after midterm pregnancy (20 weeks) and resolves after delivery. PIH is defined as raised blood pressure recorded
28 at least on two occasions at 6 hours apart (2). It may be either diastolic >90 mm of Hg or systolic >140 mm of
29 Hg. Preeclampsia is also associated with significant proteinuria >300 mg/ 24 hours (3).

31 Gestational hypertension shows an exaggerated B.P. reference detected first time after mid pregnancy without
32 proteinuria. It is thought that preeclampsia develop when the pregnancy induced systemic response causes one or
33 more maternal system to decompensate. In its clinical phase preeclampsia is a hypocalciuric state and it has been
34 reported that hypocalciuria predicts preeclampsia (9). The pregnant women's body provides daily doses of 50-330
35 mg calcium to supports development of foetal skeleton (7). This high foetal demand for calcium is facilitated by
36 profound physiological interactions between mother and foetus. Studies of blood calcium level during pregnancy
37 found significantly decreases in total serum as pregnancy progressed (6). Regulation of intracellular calcium plays
38 a key role in hypertension half of the pregnant women with hypertension have preeclampsia. Pregnant women
39 who develop severe preeclampsia have significant low dietary calcium intake compared to normotensive women. A
40 calcium supplement has been hypothesized to reduced chances of PIH and preeclampsia (16). Biochemical changes
41 in PIH are increased plasma Creatinine, urea and uric acid concentration with proteinuria due to renal glomerular
42 endotheliosis leading to impaired glomerular perfusion and filtration. Many studies have been conducted to rule

5 RESULTS

43 out the etiology , early screening and diagnostic tests, like lipid profile, oxidant and antioxidant status but
44 among these serum and urine calcium levels and calcium metabolism have been studied extensively in PIH and
45 preeclampsia and various conflicting results are given. Study is conducted to know alterations in serum and
46 urinary calcium levels in all PIH cases of hypertension induced in pregnant women in and around Chitradurga.

47 2 II.

48 Materials and Methods a) Inclusion Criteria 50 pregnant women at period (18-20 weeks) of gestation both from
49 out patients and inpatient of BMC Hospital who were following up with their with regular antenatal checkups,
50 followed with regular routine blood and Urine investigations -i.e. Hb, RBS, VDRL, urine routine examination
51 for protein, sugar, pus cells, epithelial cells are examined.

52 3 b) Exclusion criteria

53 Pregnant women who are previously known diabetic, hypertensive and suffering from any illness (mainly renal
54 and hepatic) are excluded from the study.

55 i.

56 Methods Study group will be followed up every four weeks from 28th week of gestation and 24hour/random
57 urine sample will be collected for Biochemical evaluation of urinary Calcium (12), Creatinine (13) and protein
58 by multiple strips (dipsticks) by Roche's Urine Analyser.

59 3 ml venous blood sample was collected from both PIH cases and normal pregnant women as per the criteria
60 into plane vaccutainers. Blood samples are used for serum Calcium (12), serum Uric acid (14) and serum
61 Creatinine (13). The results were statistically analysed with Students "t" test".

62 A case control comparative study was done with PIH and normal pregnant women accordingly to the criteria.

63 4 III.

64 5 Results

65 The present study included a total number of 100 subjects consists of 50 PIH cases and 50 normal pregnant
66 women. The Urinary protein levels in PIH cases is significant increase ($p<0.001$) as compared to normal pregnant
67 women. The proteinuria in PIH cases as compared to normal pregnant women is probably due to renal glomerular
68 endotheliosis leading to impaired glomerular perfusion and filtration.

69 Total protein excretion in urine is considered as abnormal in pregnant women when it exceeds 300mg/24 hours.

70 The urinary creatinine levels in PIH cases decreased as compared to ($p<0.001$) normal pregnant women. GFR
71 and renal blood flow raised markedly during pregnancy results in physiological fall in the serum Creatinine
72 concentration. Urine protein excretion increases substantially due to combination of increased GFR, increased
73 permeability of glomerular basement membrane. The protein/Creatinine ratio in PIH cases is marginally
74 increased as compared to normal pregnant women. Thus the pathogenesis of hypocalciuria in PIH is controversial
75 and theoretically may be due to decreased calcium uptake by the foetus and/or increased renal tubular absorption
76 of calcium (5).

77 The serum uric acid levels are significantly increased ($p<0.001$) in PIH cases compared to normal pregnant
78 women (Table -2) and this supports the theory of uric acid role in vascular damage and in oxidative stress, the
79 renal lesion of glomerular endotheliosis is mostlikely caused by circulating anti endothelial factors such as soluble
80 fms-like tyrosinekinase-1, it is conceivable that uric acid may synergise with soluble fms-like tyrosinekinase-1, to
81 induce endothelial dysfunction also the afferent arteriolar disease is seen in individuals with PIH, which explains
82 development of hypertension in PIH (4).

83 In this study, it was found that significant hypocalciuria was associated with preeclampsia, suggests that,
84 calcium measurement may be useful in screening for the PIH cases.



Figure 1:

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Parameter	Uriney Cal- cium	Uriney Protein	Urinary Creati- nine	and Normal pregnant women Protein/Creatin
Normal pregnant women (n=50)	390.42 ± 34.36	0.080 0.026	1.29 0.33	0.05 0.03
PIH Cases (n=50)	342.92*** ± 52.1	0.333*** 0.13	± 0.76** ± 0.11	0.43* ± 0.17

Note: 1. The number in parenthesis shows the number of samples.

2. Values are expressed as their Mean \pm SD.

3. p-value * p<0.05, ** p<0.01, *** p<0.001.

Table -2 shows, the serum levels of Uric acid, Calcium and Creatinine in PIH cases and compared with normal pregnant women.

Figure 2: Table 1 :

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2

Parameter	pregnant women			
	Serum acid (Mg/dl)	Uric acid (Mg/dl)	Serum Calcium (Mg/dl)	Serum Creatinine (Mg/dl)
Normal pregnant women (n=50)	5.62 ± 1.01		8.95 ± 0.88	0.80 ± 0.13
PIH Cases (n=50)		7.64*** ± 1.39	8.29** ± 0.47	0.898 ± 0.16

Note: 1. The number in parenthesis shows the number of samples.

2. Values are expressed as their Mean ± SD.
3. p-value * p<0.05, ** p<0.01, *** p<0.001.

Figure 3: Table 2 :

Figure 4: Table - 1

85 [Kumar] , Kumar . New Delhi: Jaypee Publications. p. . (1st Edn)

86 [Edn et al.] , ; Edn , T M Da Warrel , J P Cox , Firth . New York: Oxford University press. 2 p. .

87 [Young ()] , D S Young . *Clin. Biochem. Revs* 1982. (4) p. .

88 [Sanchez-Ramos et al. ()] 'Calcium excretion in preeclampsia'. L Sanchez-Ramos , S Sandroni , F J Andres . *J Obstet Gynecol* 1991. 77 p. .

89 [Varley et al.] *Determination of Creatinine in Urine*" practical Clinical Chemistry, H Varley , A H Gowenlock , M Bell . 1 p. . (4th edn)

90 [Varley et al.] *Determination of serum calcium and Urinary Calcium* "practical Clinical Chemistry, H Varley , A H Gowenlock , M Bell . p. . (4th edn)

91 [Redman ()] 'Hypertension in pregnancy'. C W G Redman . *Oxford textbook of medicine*, 2003. p. 4.

92 [Chatterjee and Basu ()] *Hypertensive disorders in pregnancy*" in *Essentials of Obstetrics, Arulkumaran S, Sivanesarantnam V, and Pratap In a conclusion, hypocalciuria and hyperproteinuria is important feature of severe preeclampsia and probably indirectly related to the altered renal function seen in toxæmia of pregnancy*, A Chatterjee , Githa Basu . 2004.

93 [Taufield et al. ()] 'Hypocalciuria in preeclampsia'. P A Taufield , K L Ales , L M Resnick . *N. Engl J Med* 1987. 316 p. .

94 [Frankle et al. ()] 'Hypocalciuria of preeclampsia is dependent of parathyroid hormone'. Y Frankle , G Barkai , S Mashiach . *Obstet Gynecol* 1991. 77 p. .

95 [Kova and Berg ()] 'Maternalfetal Calcium and Bone Metabolism during pregnancy, Puerperium and Lactation'. C S Kova , Keronen Berg , HM . *Endocrine Reviews* 1997. 18 (6) p. .

96 [Landing and Annpyankubas ()] 'Randomised plasibo Controlled Calcium Supplementation Study in pregnant Gambian women'. M A Landing , Annpyankubas . *American Journal of Clinical Nutrition* 2006. 83 (30) p. .

97 [Ramos et al. ()] 'Reported Calcium intake is reduced in women with preeclampsia'. J G Ramos , E Brietzke , Martins-Costa , Sh . *Hypertens pregnancy* 2006. 25 (3) .

98 [Chunlam et al.] 'Uric acid and Preeclampsia'. Kee-Hak Chunlam , Dukhee Lim , S Anath Kang , Karumanchi . *Seminars in Nephrology*. Pg p. .

99 [Suarez et al. ()] 'Urinary calcium in asymptomatic primigravida who later developed preeclampsia'. V R Suarez , J G Trelles , J M Miyahira . *J. Obstet. Gynecol* 1996. 87 p. .

100 [Bilgin et al. ()] 'Urine calcium excretion in preeclampsia'. T Bilgin , O Kultu , Y Kimya . *T kin J Obstet Gynecol* 2000. 10 p. .

101 [Yoshida et al. ()] A Yoshida , K Morozumi , T Suganuma , K Sato , J Aoki , T Olkava , T Pujinami . *Urinary Calcium References Références Referencias*, 1989.

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