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MATERNAL SERUM CALCIUM AS A PREDICTOR OF PREECLAMPSIA- A CASE CONTROL STUDY

Janki dosad[1], Dr.nidhi Bahuguna[2] ,Dr.neha kakran[3], Dr.arjun singh doshad[4] ,Dr.ravinder bisht[5]

Aim- To compare the levels of serum calcium in preeclampsia patients and normotensive singleton pregnant women.

Introduction- Preeclampsia is a syndrome universally defined by the onset of hypertension (≥140/≥90mmHg) and proteinuria (≥0.3g/24h) after 20 weeks of gestation in a previously normotensive woman. An association has been found between pre-eclampsia and hypocalciuria; lower urine calcium to creatinine ratio; lower dietary milk intake; and between eclampsia and hypocalcaemia The present study aim is to evaluate the predicative value of serum calcium in preeclampsia patients so that timely intervention can be done and subsequent complications can be prevented.

Material and Method- This study was conducted during the period of December 2018 to June 2019 at Department of obstetrics and gynaecology, SMI Hospital, Patelnagar, deharadun. It was a case control prospective study. A total 80 pregnant female of which 40 patients with preeclampsia as a case and 40 patients without preeclampsia were selected as control for the study.

Result-. In our study there was statistically decreased levels of serum calcium in cases ($P < 0.001$). The diagnostic accuracy in cases was 80% and there was highly significant negative correlation between serum calcium and Diastolic blood pressure.

Conclusion- In our study we found that serum calcium levels were significantly reduced in preeclamptic patients suggesting that serum calcium may have a role in the etiopathogenesis of this disorder. Therefore, we concluded that serum calcium could be considered as a supportive diagnostic tool in preeclampsia along with other biochemical markers.

Key words- serum calcium , preeclampsia,

INTRODUCTION-

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection, that contribute greatly to maternal morbidity and mortality. How pregnancy incites or aggravates hypertension remains unsolved despite decades of intensive research. Indeed hypertensive disorders remain among the most significant and intriguing unsolved problems in obstetrics.(1)

Preeclampsia is a multi-system disorder that complicates 3-5% of pregnancies in western countries and constitutes a major source of morbidity and mortality worldwide. (2,)

Overall, 10 to 15% of maternal deaths are directly associated with preeclampsia and eclampsia.(3) Preeclampsia is a syndrome universally defined by the onset of hypertension

(≥140/≥90mmHg) and proteinuria (≥0.3g/24h) after 20 weeks of gestation in a previously normotensive woman.There is a relationship between placental insufficiency and the pathophysiology of preeclampsia. Placental oxidative stress plays an important role in the manifestations of preeclampsia.(4)

An inverse relationship between calcium intake and hypertensive disorders of pregnancy was first described in 1980 (Belizan1980). This was based on the observation that Mayan Indians in Guatemala, who traditionally soak their corn in lime before cooking had a high calcium intake and a low incidence of pre-eclampsia and eclampsia and a very low prevalence of pre-eclampsia had been reported from Ethiopia where the diet, contained high levels of calcium.

There were many hypothesis states that an increase in calcium intake during pregnancy might reduce the incidence of high blood pressure and pre-eclampsia among women. (5,6)

An association has been found between pre-eclampsia and hypo-calciuria; lower urine calcium to creatinine ratio; hypo-calcaemia; lower plasma and higher membranous calcium; lower dietary milk intake; and between eclampsia and hypo-calcaemia. (7)

Low calcium intake may cause high blood pressure by stimulating either parathyroid hormone or renin release thereby increasing intracellular calcium in vascular smooth muscle and leading to vasoconstriction.

A calcium supplementation reduces parathyroid release and intracellular calcium and so reduces the uterine smooth muscle contractility and prevent preterm labour and delivery.(8)Calcium also have an indirect effect on smooth muscle function by increasing magnesium levels. Blood calcium and magnesium have a relaxant effect on the blood vessels of pregnant women.(9) Supplementation in the second half of pregnancy appears to reduce blood pressure directly rather than preventing the endothelial damage associated with pre-eclampsia. Calcium supplementation may play a beneficial role in the prevention of PIH by maintaining plasma ionized calcium levels within the narrow physiological range.

Maintaining this range is crucial for the ongoing synthesis of vasoactive substances such as prostacyclin and nitric oxide in the endothelium and consequently for a normal endothelial function and thus lowering the blood pressure.

Therefore, understanding of the underlying factors that explain the pathogenesis of pre-eclampsia and the early identification of the patients at risk of the disease will help in the development of preventative or early therapeutic interventions required to reduce the associated morbidity and mortality during pregnancy.

AIM-

1) To compare the levels of serum calcium in preeclampsia patients with normotensive singleton pregnant women.

OBJECTIVE- 1) To determine the association of serum calcium with preeclampsia.
2)screening of preeclampsia patient with respect to serum calcium level in blood.
3)timely identification and prevention of preeclampsia.

INCLUSION CRITERIA –

Cases: All singleton Pregnant female of any age irrespective of gravida in third trimester of gestation with diagnosed preeclampsia on the basis of Clinical history, examination, blood pressure >140/90 mmHg .

Controls: All singleton asymptomatic pregnant female of any age irrespective of gravida in third trimester of gestation with normal blood pressure.

EXCLUSION CRITERIA-

- Patients with multiple gestation
- Patients in active labor
- Patients with essential hypertension
- Patients with history of all systematic diseases.
- Women with premature rupture of membranes
- Women with severe anaemia (Hb < 6g/dL)

MATERIAL AND METHOD-

Study design: comparative case control study

Study duration: six months (december 2018 to June 2019)

Place of study: This study was conducted at Department of obstetrics and gynaecology, SMI Hospital, Shri Guru Ram Rai Institute of Medical & Health sciences, Dehradun

Sample: A total 80 pregnant female of which 40 patients with preeclampsia as a case and 40 patients without preeclampsia were selected as control for the study

DATA ANALYSIS-

Measurement of Calcium

The VITROS CA Slide method is performed using the VITROS CA Slides and the VITROS Chemistry Products Calibrator Kit 1 on VITROS 50/350.

OBSERVATION AND RESULT-

This was a comparative case control study conducted on 40 patients with clinically diagnosed preeclampsia and 40 normal subjects.
Serum calcium levels were estimated, analyzed and compared with diastolic blood pressure. The results are expressed as mean ± standard deviation.

Table1.Comparison of serum calcium levels between cases and controls

Groups	**Serum calcium(mg/dl)**	
	Range	**mean±SD**
Cases	7.8-10.1	8.76±0.53
Controls	8.8-11.2	10.09±0.6
t*	10.43	
P	<0.001	

On applying unpaired t -test, we found that the mean serum calcium (mg/dL) in cases and controls were 8.76 ± 0.53 and 10.09 ± 0.6 and was highly significant. (P < 0.001) (Table 1 Figure 1)

Figure 1-Serum Calcium level in cases and controls

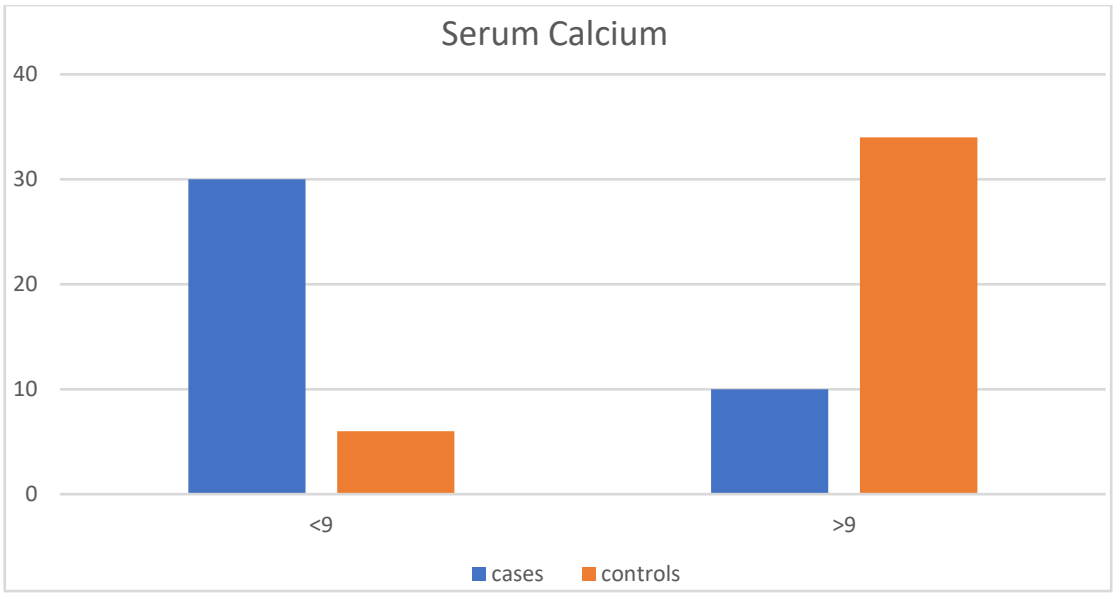


Table 2 Diagnostic Value of Serum Calcium in Preeclampsia

Serum Calcium Cut off Value : < 9mg/dl			
Serum Calcium (mg/dl)	Cases	Controls	Total
<9	30(75%)	6(15%)	36
>9	10(25%)	34(85%)	44
Total	40	40	80
$X^2 = 38.5$ P<0.001, Significant			
Sensitivity = 75% Specificity = 85% Positive Predictive Value = 83.3% Negative Predictive Value = 77.2% Diagnostic Accuracy = 80%			

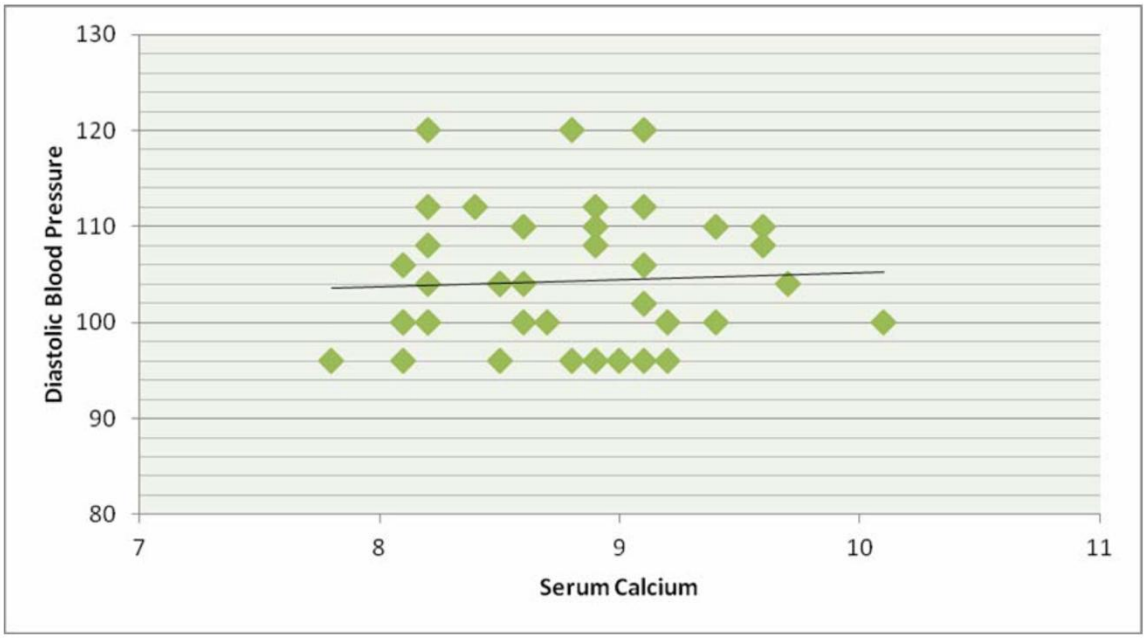
The cut off value for serum calcium was considered as 9 mg/dL and the predictive value in preeclampsia was noted. Out of 80 participents,75% of cases and 15% of the controls had serum calcium levels < 9 mg/dL while 25% of cases and 85% of controls had > 9 mg/dL which showed that this test had 75% sensitivity and 85% specificity and the positive predictive value of this test was 83.3%, the

negative predictive value was 77.2% which makes the diagnostic accuracy of the test 80% and makes the p value significant i.e p value <0.001.

Table 3.Correlation of Serum Calcium with Diastolic blood pressure in Cases

Correlation between	Pearsons Correlation Coefficient (r)	Significance	
Serum Calcium and Diastolic BP	- 0.05	P= 0.01* (p<0.05)	Significant Negative correlation

On applying pearsons correlation coefficient there was negative correlation between Serum Calcium and Diastolic BP. r = - 0.05, P = 0.01 and was highly significant.



DISCUSSION-.

As we know that preeclampsia is a complex dynamic pregnancy disorder , associated with increased maternal and fetal morbidity and mortality especially in developing countries.Serum calcium plays an important role in the uteroplacental blood flow as it lowers the resistance index in uterine and umbilical arteries and its deficiency is capable of producing smooth muscle constriction and increased vascular resistance. Lopez ,Jaramillo P95 and co-workers suggested beneficial effect of calcium supplementation to reduce the vasoconstriction and subsequent onset of preeclampsia in their epidemiological study and the explanation for the vasoconstriction due to calcium deficiency was reduced vasoactive substances. Serum calcium ion level plays a crucial role in the production of endothelial NO; the increased generation of which maintains the vasodilatation that is characteristic of normal pregnancy and the time period for the estimation of serum Ca++ should be done as early as possible, in the first or second trimester.

In this present comparative case-control study we have compared the above biochemical parameters in 40 cases with preeclampsia and 40 apparently healthy age and gestational age matched normal singleton pregnant controls. The significance of serum calcium between the two groups, their diagnostic value and correlation with diastolic blood pressure is analyzed and discussed. We found that there were statistically decreased levels of serum calcium in cases ($P < 0.001$) and the diagnostic accuracy in cases was 80% and there was highly significant negative correlation between serum calcium and Diastolic blood pressure. Similar study done by Sukonpan K et al,32 Idogun E S et al,97Akthar R et al,109 where they found a significant decrease in serum calcium levels not only in cases of preeclampsia but also showed inverse correlation with severity of preeclampsia.(10)

Another similar study done by sunita M aghade et al they showed the similar result of serum calcium and its negative correlation with systolic/diastolic blood pressure in preeclamptic

women and suggested a strong association between deficiency of this mineral and the outset of preeclampsia.(11).
Another study done by Ismail A(12) and his colleagues found hypocalcemia in all the studies from developing countries in a metaanalysis which explained its contribution as a risk factor for developing preeclampsia. Therefore they suggested that calcium has to be supplemented in every pregnancy and the dosage used was not empirical but was based on individual patient requirement. Similar study done by Hofmeyr G J et al107 where they concluded that calcium supplementation appears to approximately half the risk of pre-eclampsia and therefore reduce the risk of preterm birth .

CONCLUSION-

In our study we found that serum calcium levels were significantly reduced in preeclamptic patients thus suggesting that serum calcium may have a role in the etiopathogenesis of this disorder and calcium supplementation may play a beneficial role in the prevention of PIH by maintaining plasma ionized calcium levels within the narrow physiological range of oxidative stress, inflammation and NO deficiency induced vasoconstriction.This supports the hypothesis that hypocalcemia may have role in the etiology of preeclampsia and dietary interventions may reduce the preeclampsia risk. Thus, it can be concluded that serum calcium could be considered as a supportive diagnostic tool in preeclampsia along with other biochemical markers and it should be regularly supplements in pregnant women routinely.

CONFLICTS OF INTEREST-nil

FINANCIAL SUPPORT AND SPONSORSHIP-nil

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- 1-Author-Janki dosad, Demonstrator, Department of Biochemistry, Veer Chandra Singh Government Medical Science And Research Institute Srinagar, Uttarakhand, email id-doshadjanki24@gmail.com
- 2-Dr. nidhi bahuguna, Senior resident, , Department of obstetrics and gynaecology, Veer Chandra Singh Garhwali Government Medical Science And Research Institute Srinagar, Uttarakhand, email id-ndhbahuguna@gmail.com

- 3-Corresponding author- Dr.neha kakran, Assistant professor, Department of obstetrics and gynaecology, Veer Chandra Singh Garhwali Government Medical Science And Research Institute Srinagar, Uttarakhand , email id-neha.kakran44@gmail.com phone no-9267985321

- 4-Dr.Arjun singh doshad, Assistant professor,Department of ENT, Veer Chandra Singh Garhwali Government Medical Science And Research Institute Srinagar, Uttarakhand, email id-arjun.msent@gmail.com phone no-8057728897

5- Dr. Ravinder singh bisht, professor, Department of ENT, Government Doon Medical college,Uttarakhand, email id- Dr_rsbisht@rediffmail.com