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Original Research Article

Serum Calcium Levels in Hypertensive Disorders in Pregnancy and it's effect on Fetal Outcome in a Tertiary Care Center in Central India

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Abstract

Background: Calcium requirement increases during pregnancy, thereby increasing the chances of developing hypocalcaemia. Hypocalcaemia may be associated with pregnancy-related complications. Therefore, this study aim to estimate the prevalence of hypocalcaemia among Normotensive and Hypertensive pregnant women, and to study association between hypocalcaemia and fetal outcomes.

Aim & Objective: To study levels of calcium in hypertensive and Normotensive antenatal patients and it's affect on fetal outcome.

Methods: It is a case control study. Data about hypertensive and Normotensive antenatal patients is being collected from their admission at hospital, their serum calcium levels done. Their fetal outcome have been studied on basis of their follow-up.

Settings and Design: This study was done in a medical college hospital in Madhya Pradesh.

Results: 240 antenatal patients were labelled as Normotensive and Hypertensive, they were followed up till delivery. Prevalence of hypocalcemia in hypertensive pregnant patient was slightly Higher than in Normotensive antenatal patients. Also serum calcium level among pregnant women who delivered LBW baby was lower than those who delivered baby with birth weight >2500 grams.

Conclusion: It has been concluded in this study that serum calcium levels were reduced in hypertensive as compared to normotensive antenatal patients. LBW was associated with low serum calcium level. The actual role of calcium supplements needs further investigation.

Introduction

Preeclampsia is a disease with worldwide significance to mothers and infants and it is a leading cause of death and disability in mothers and infant[1]. It is a multiorgan disease that affects about

6% of all pregnancies [2]. It is a rapidly progressive condition .[3]. Sudden weight gain, headaches and changes in vision are important warning symptoms. Typically blood pressure elevations happens in the late second trimester or third trimester [4]. The pathophysiological mechanism most likely cause it is characterized by a failure of the trophoblastic invasion of the spiral arteries which inturn increases vascular resistance of the uterine artery and a decreased perfusion of the placenta .The incidence is about 5-7% in primigravid women [5]. It may be associated with complications like visual disturbances, oliguria, eclampsia, hemolysis, elevated liver enzymes, thrombocytopenia,

pulmonary oedema and fetal growth restriction [7]. Early detection and prompt management helps in reducing the complications and improving fetal outcome. Despite its prevalence and severity, the patho physiology of this multisystem disorder is still poorly understood and its aetiology has not yet been fully explained [8]. Multiple studies have shown that Environmental and nutritional factors may play a significant role in the aetiology of pre-eclampsia.

Nutritional deficiencies of both macro and micronutrients are more evident in women of reproductive age group, commonly in developing countries[9]. Epidemiological and biological evidence suggest that acute or chronic specific nutritional deficiencies can contribute to severe maternal morbidity. Pregnancy is a period of increasing metabolic demands with changes in a women's physiology and the requirements of a growing fetus. An inadequate intake might be harmful not only for the mother but also for the fetus and it's growth[10].

Hypertensive disorders account for around 40,000 maternal deaths annually [11]. Therefore, to reduce the risk of hypertensive disorders in pregnancy, most researches are focusing on prevention rather than treatment. A role of altered calcium metabolism in the pathogenesis of pre-eclampsia has been suggested based on epidemiological evidence linking low dietary levels of calcium and increased incidence of the disease [12].

Calcium deficiency may cause increased blood pressure, this phenomenon is partially explained by calcium-magnesium exchange, the primary factor involved appears to be parathyroid hormone, since magnesium deficiency impairs both the release of parathyroid hormone and its uptake by bone and skeletal end organ [10,1,13]. Calcium and Magnesium plays an important role in peripheral vasodilatation [13]. However, the role of calcium and magnesium in pregnant women are still under study. The aim of this study is to measure serum levels of calcium in Hypertensive Disorders of Pregnancy and to compare with those in normal pregnancy and it's effect on Fetal outcome

Materials and Methods

This was a case-control study conducted to investigate the levels of calcium and magnesium in pregnant women with and without hypertensive disorders of pregnancy. The study population was pregnant women attending the antenatal clinic and admitted in the obstetric ward in the Department of Obstetrics and Gynaecology in a teaching hospital in Indore, Madhya Pradesh. India is a developing country where the nutrition of pregnant women is a matter of concern. 240 women were included in the study, of whom 120 were with Hypertensive and the other 120 were normal pregnant women without pre-eclampsia who were taken as controls. All participants were in the third trimester of pregnancy with a gestational age of more than 32 weeks, primi or multigravida and . Cases and controls were matched for gestational age, parity, anthropometrics and socioeconomic status. Most of the women were from the lower middle class strata with poor dietary consumption of calcium and magnesium rich food. Pre-eclampsia was diagnosed in a women who had a blood pressure of 140/90 or more on two occasions each 6 hours apart associated with proteinuria of at least 300 mg per 24 hours or at least 1+ on dipstick testing. Severe pre-eclampsia was defined as a blood pressure of 160/110 mm Hg or above measured on two occasions each 6 hours apart. The repeat measurement of blood pressure was done in the hospital after adequate rest. The women were selected following medical examination and investigations.

Informed consent was obtained from each of the subjects before recruiting in to the study.

Patients with history of chronic hypertension, renal disease, cardiovascular

disease, liver disease, diabetes, thyroid and other endocrine disorders, , hydatidiform mole and other secondary causes of hypertension, malignancy, hematological disorders etc were excluded from the study. Also women with history of smoking, alcohol and other drug consumption which might affect the blood pressure were excluded from the study. A detailed family and medical history were taken. Thorough clinical examination was done in all the subjects. Systolic and diastolic blood pressure was carefully recorded. Urine analysis was done in all subjects to measure the degree of proteinuria. Blood was taken from the ante cubital vein using a sterile needle and syringe. Blood samples were allowed to clot and then centrifuged at 3000 revolutions per minute for 10 minutes. Comparison of serum calcium levels of the elements between the two groups was performed by Unpaired t-test and p-value of < 0.05 was considered as statistically significant.

Results

This prospective study was carried out at MYH and MTH hospital, Indore in 240 pregnant patient admitted in our department of obstetrics and gynaecology. They were equally divided into 2 groups based on their blood pressure at the time of admission.

Table 1: Study population

S. No.	Category	No of women	Percentage
1	Study group	120	50
2	Control group	120	50

Among 240 pregnant women who had BP >_140/90 mm of Hg at the time of admission were placed in study group and those having Blood pressure < 140/90 were placed in control group.

Table 2: Age distribution

S. No.	Age(in years)	Control group	Study group
		n (%)	n(%)
1	<20	10(8.3%)	15(12.5%)
2	21-25	72(60%)	78(65%)
3	26-30	26(21.6%)	14(11.6)
4	>30	12(10%)	13(10.8%)

Among the control group most of the cases were in the age group 21-25 years followed by 26-30 years and remaining were more than 31 years.

Among the study group 12.5% were of age less than 20 years and 10.8% were more than 31 years. This observation shows that either end of reproductive age are more susceptible of preeclampsia. Youngest in this study was 18 years and eldest was 38 years. Most of the cases were in the age group 21 - 25 years.

Table 3: Parity

S. No.	Parity	Control group	Study group
		n(%)	n(%)
1	Primi	70(58.3%)	80(66.6%)
2	G2	34(28.3%)	24(20%)
3	G3	08(6.6%)	12(10%)
4	G4	08(6.6%)	04(3.33%)

Among the control group 58.3% were Primi, 28.3% were 2nd gravida, 6.6% 3rd gravida and 6.6% were 4th gravida.

Among the study group 66.6% were primi. This is in conformity with the general incidence of preeclampsia. 24% were 2nd gravida, and remaining were 3rd and 4 th gravida.

Table 4: Socioeconomic status

S. No.	Socio economic status	Control group n(%)	Study group n(%)
1	Class I	-	
2	Class II	-	
3	Class III	-	
4	Class IV	08(6.6%)	06(5%)
5	Class V	112(93.3%)	114(95%)

Among the control group 93.3% were in class V socio economic status, 6.6% were belonging to class IV socioeconomic status**.**

Among the study group 95% were belonging to class V socioeconomic status and 5% were from class IV socio economic status. This is in expected lines since our hospital essentially caters to population who were below poverty line.

Table 5: Levels of S. calcium and it's compatible with the control group

S. No.	Category	Number	S. Ca levels ± Standard Deviation	Unpaired T- Test values	P value
1	Control group	120	7.825 ± 0.714	7.886	< 0.001
2	Case group	120	6.826± 0.623		

The mean values of A. Calcium in the control group is 7.825±0.714 meq/L whereas in study group is 6.826 ± 0.623 meq/L.

The mean values of S. Calcium is statistically significantly lower in study group as compared to the control group

Table 6: Blood pressure distribution

S. No.	Blood pressure	Frequency	Percentage
1	Systolic -100 to 128	120	50%(allthe
	Diastolic – 70-80		Normotensive group/control group)
2	Systolic – 130 to 158	103	42.5%
	Diastolic – 90 to 108		
3	Systolic - >160	17	7.5 %
	Diastolic - >110		

Of the 240 pregnant women who participated in this study, 120(50%) were normotensive with systolic BP in the range of 100 - 128 mm Hg, Diastolic BP 70 - 88 mm Hg, 42.5 % were diagnosed as mild pregnancy induced Hypertension with systolic BP in the range of 130 - 158 mm Hg and diastolic BP 90 - 108 mm Hg.

7.5% developed severe pregnancy-induced hypertension with the BP range ≥ 160 / 110 mm Hg.

Table 7: Distribution with respect to Birth weight

S. No.	Group	Birth weight	Frequency	Percentage
1.	Control group	<2kg	11	9.5%
		2 to 2.5 kg	55	45.8%
		>2.5 kg	54	45.6%
2.	Study group	< 2 kg	12	9.6%
		2 to 2.5 kg	67	55.8%
		>2.5 kg	41	34.16%

In control group the mean value of S.Calcium in Mother's of baby weighing<2.5 kg is 6.365 (which is >2SD of the control group) .
In study group the calcium levels are generally low in all distributions.

Discussions

Nutritional deficiencies are common during pregnancy. Pregnant women in developing countries have been reported to consume diets that are low in minerals and vitamins [4]. Dietary deficiencies of calcium and magnesium during pregnancy is considered in pathogenesis of pre-eclampsia, eclampsia, preterm birth and intrauterine growth retardation [10]. Calcium is the micronutrient that has been best studied to be associated with pre-eclampsia. These observations led to the hypothesis that the incidence of pre-eclampsia can be decreased in populations of low calcium intake by calcium supplementation [9].An inverse relationship between calcium intake and hypertensive disorders of pregnancy was first described in 1980 based on the observation that Mayan Indians in Guatemala had a low incidence of pre-eclampsia as their intake of calcium was high due to the traditional method of cooking with lime [22]. Similarly,Mahomed et al., reported a decreased intake of calcium during pregnancy in many different parts of the world such as Asia, Latin America, and Africa as well as developed countries such as Canada, USA and the UK. They also reported decreased intake of calcium in India. (250mg/d) [23]. Calcium plays a significant role in muscle contraction and modification of plasma calcium concentration leads to changes in blood pressure. The lowering of serum calcium can cause an elevation of blood pressure in preeclamptic mothers. The increase of cellular calcium concentration when serum calcium decreases led to constriction of smooth muscles in blood vessels and increase in vascular resistance [1].

Punthumapol and Kittichotpanich showed that serum calcium in severe pre-eclamptic women was lower than normal pregnant women and mild pre-eclamptic women respectively but no difference in serum magnesium levels [13].

Similarly, Kumru et al., in their study found significantly lower levels of calcium (10%) in pre-eclamptic women compared to healthy controls, with no significant difference in magnesium levels. They concluded that measurement of these elements may be useful as a predictor of a preeclamptic condition [5]. Akhtar S et al., in a study from Bangladesh showed significantly lower levels of calcium in pre-eclamptic women [15]. They gave an opinion that early detection and supplementation to treat this deficiency may reduce the incidence of pre-eclampsia. Akinloye et al., in a study from Nigeria reported a decrease in serum magnesium in pregnant women with pre-eclampsia [4].

A Cochrane review analysed 12 high quality trials after excluding 24 trials on supplementation of calcium to prevent pre-eclampsia in normotensive pregnant women. The dose of calcium evaluated was 1.5 to 2 gm daily. There was less high blood pressure associated with calcium supplementation rather than placebo. Calcium supplementation appeared to approximately half the risk of preeclampsia. The reduction was greatest for women at high risk of developing pre-eclampsia and for those with low baseline dietary calcium. The Relative Risk of having the composite outcome maternal death or serious morbidity was reduced for women allocated calcium supplementation compared with placebo. The review commented that adequate dietary calcium before and in early pregnancy may be needed to prevent the underlying pathology responsible for preeclampsia. They also suggested that the research agenda should be redirected towards

calcium supplementation at a community level [25].

We conducted this study to find out the serum levels of calcium and Hypertensive Disorders of Pregnancy and normal pregnancies and to evaluate the association between these elements and PIH. There was a significant reduction in calcium levels in Hypertensive pregnant women compared to normotensives. This study also concludes that low level of serum calcium in Mothers are associated with low birth weight in baby.

According to the results of our research, intake of calcium supplements may help in the reduction of incidence of pre-eclampsia especially in a population of a developing country like ours where the nutrition is poor. Chaurasia et al., found significantly lower levels of serum calcium and magnesium in pre-eclamptic women compared to normal pregnant women [20]. Another study by Sandip et al., found significantly lower levels of calcium and magnesium in severe pre-eclamptic women compared to normotensive and mild pre-eclamptic women[26]. Limited data is available on the role of calcium and magnesium from rural south India where the diet is deficient of the necessary elements. High risk women with low calcium and magnesium intake will be benefited with supplementation. Milk, soy milk, yogurt, cheese and vegetables like cabbage, broccoli, almonds, sardine and salmon with bones and calcium fortified orange juice are good sources of calcium. Foods rich in magnesium include whole grains, nuts and green vegetables. Green leafy vegetables are particularly good sources of magnesium. The limitation of our study was that a detailed dietary assessment of the subjects was not done. Pregnant women in developing countries should be encouraged to consume food rich in calcium and magnesium. If the intake is less than the recommended dose, a supplement can be given to benifit them.

Conclusion

To conclude, our study shows a significant reduction of serum calcium levels in Hypertensive pregnant women compared to normotensives. This supports the hypothesis that hypocalcemia may have a role in the aetiology of pre-eclampsia. Further trials are needed regarding the role of calcium and magnesium supplementation in prevention of pre-eclampsia. This study also concludes that low level of serum calcium in mothers are associated with low birth weight in baby.

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