

A Hospital Based Analytical Assessment of the Association of Serum Calcium and Serum Magnesium in Gestational Hypertension and Pre-Eclampsia

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Abstract

Aim: The aim of the present study was to evaluate the level of serum calcium and serum magnesium in pregnancy induced hypertension and normal pregnancy.

Methods: The present study was conducted in the Department of obstetrics and Gynaecology, Shahid Nirmal Mahato Medical College & Hospital, Dhanbad Jharkhand From 01.04.2020 to 31.03.2021 and 100 women were included in the study. Data for the study was collected from 50 normotensive normal pregnant women with more than 20 weeks of gestational age (control group) and 50 pregnancy induced hypertension patients (study group) attending for the antenatal care in Department of Obstetrics and Gynecology in Shahid Nirmal Mahato Medical College & Hospital, Dhanbad. (Jharkhand).

Results: A comparative clinical study (case-control study) with 50 patients (PIH) and 50 normal pregnant women is undertaken to study the serum calcium and serum magnesium the present study was well matched in age between both groups and comparable with the mean age in study group 22.88 ± 2.28 years, control group 23.87 ± 4.25 . Majority of patients are in 21-25 year group in both study (44%) and controls (52%). Mean systolic blood pressure in study group was 150.34 ± 9.91 mmHg and in controls 114.86 ± 8.22 mmHg. Mean diastolic blood pressure in study group was 100.40 ± 9.21 mmHg and in controls 74.64 ± 6.14 mmHg. The result showed the concentration of serum calcium in controls as 9.11 ± 0.82 and in study group 8.12 ± 0.37 mg/dl with P value <0.001 . The serum magnesium levels in controls 2.08 ± 0.46 and in study group was 1.79 ± 0.70 mEq/L with P value 0.012. The serum calcium and magnesium has significantly decreased in cases compared to controls.

Conclusion: The study data supported the hypothesis that calcium and magnesium deficiency might be the cause in the development of preeclampsia. The consequence of the deficiencies of the calcium and magnesium may be responsible for the clinical manifestations that are observed in preeclampsia and eclampsia patients since both ions are important in cellular and neuronal metabolism as well as cell membrane stability.

Keywords: Serum calcium, Serum magnesium, Pregnancy induced hypertension, Normal pregnancy

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Introduction

Pre-eclampsia is one of the most common causes of maternal and fetal morbidity and mortality. [1] It is a systemic disease that affects about 5 – 7 % of all pregnancies and is the most common, yet least understood disorder of pregnancy. [2] It is a rapidly progressive condition characterized by high blood pressure, platelet aggregation, swelling of the lower extremities and protein in urine. [3] Sudden weight gain, headaches and changes in vision are important symptoms. Typically blood pressure elevations and pre-eclampsia occur in the late second trimester or third trimester. [4] The pathophysiological mechanism is characterized by a failure of the trophoblastic invasion of the spiral arteries which may be associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta. [1] The incidence is about 6% in primigravid women. [5] Clinically pre-eclampsia is characterized by persistently elevated blood pressure of greater than 140/90 mmHg, proteinuria and oedema. [6] It may be associated with complications like visual disturbances, oliguria, eclampsia, hemolysis, elevated liver enzymes, thrombocytopenia, pulmonary oedema and fetal growth restriction. [7]

The term pregnancy induced hypertension is quite commonly used and encompasses hypertension, either with proteinuria (Preeclampsia) or without proteinuria (gestational hypertension). [8] In this study the word preeclampsia is used synonymously with pregnancy induced hypertension. A number of dietary deficiencies or excesses have been blamed as the cause for preeclampsia over centuries.

Pregnancy is a period of high calcium demand because of fetal requirement. Pregnancy entails number of physiological events with implications regarding calcium

metabolism: the extracellular fluid expands, the albumin level decreases, the glomerular filtration rate increases causing increase in calciuria and calcium is removed from the maternal system by transfer to fetus. These mechanisms all tend to promote lowering of maternal calcium concentration and present pregnant women for maintaining the levels within the narrow range necessary to preserve homeostasis. [9,10] On the physiological basis, calcium plays an important role in muscle contraction and regulation of water balance in cells. Modification of plasma calcium concentration leads to alteration of blood pressure. The lowering of serum calcium and the increase of intracellular calcium can cause an elevation of blood pressure in preeclamptic mothers. [11] Generally hypomagnesaemia in most of pregnant women is associated with haemodilution, renal clearance, consumption of minerals by the growing fetus. There is decrease in ionized and total magnesium levels with increasing gestational age during normal pregnancy, as well as evidence of magnesium disturbance in women who later developed pre-eclampsia. Magnesium levels may have significant effects on cardiac excitability and on vascular tone, contractility and reactivity. Magnesium causes vascular muscle relaxation. [12,13] Pregnancy induced hypertension is characterized by vasospasm, elevated blood pressure and increased neuromuscular irritability, features common to syndromes of magnesium deficiency. [14]

The aim of the present study was to evaluate the level of serum calcium and serum magnesium in pregnancy induced hypertension and normal pregnancy.

Methods

The present study was conducted in the Department of Obstetrics and Gynaecology, Shahid Nirmal Mahato

Medical College & Hospital, Dhanbad, Jharkhand From 01.04.2020 to 31.03.2021. 100 women were included in the study. Data for the study was collected from 50 normotensive normal pregnant women with more than 20 weeks of gestational age (control group) and 50 pregnancy induced hypertension patients (study group) attending for the antenatal care in Department of Obstetrics and Gynecology in Shahid Nirmal Mahato Medical College & Hospital, Dhanbad. (Jharkhand). Cases were selected randomly. Serum calcium and Serum magnesium levels were estimated by spectrophotometry method. Cases and controls were matched as far as possible.

Inclusion criteria

Study group:

1. Diagnosed pregnancy induced hypertension based on criteria - blood pressure $\geq 140/90$ mmHg on two separate occasions 6 hours apart, Proteinuria more than 300 mg in 24 hour urine or 1+ dipstick in two midstream urine samples collected 4 hours apart, with or without edema, in more than 20 weeks gestational age.

2. Singleton pregnancy

3. Age 15-40 years

4. Non diabetic

Control group:

1. More than 20 weeks gestational age

2. Singleton pregnancy

3. Age 15-40 years

4. Non diabetic

Exclusive criteria

1. Chronic hypertension

2. Gestational diabetes mellitus

3. Renal disease

The subjects included in this group were out patients and inpatients of above mentioned hospital. Patients were selected

for the study based on the inclusion criteria and by subjecting them to history taking, clinical examination - general physical examination, vitals, systemic examination. The study protocol was approved by the ethical committee and written informed consent was obtained from each woman before inclusion in the trial.

Collection of blood samples

About 5 ml of venous blood was collected in a clean and dry centrifuge tubes. Blood was allowed to clot; serum was separated from the clot by centrifugation. Serum calcium and magnesium was measured by spectrophotometry. Serum calcium estimation Normal range of serum calcium is 8.4-10.4 mg/dl, or 4.25-5.2 mEq/L Methodology: Arsenazo III method, end point Principle: Arsenazo III combines with calcium ions at pH 6.75 to form a coloured chromophore, the absorbance of which is measured at 650 nm (630-660nm) and is proportional to calcium concentration. Arsenazo III has a high affinity for calcium ions and shows no interference from other cations normally present in serum, plasma, urine. Calculations for serum calcium (mg/dl) = (Absorbance of test/Absorbance of standard) \times Concentration of standard (mg/dl) SI conversion factor: 1mg/dl = 1 mmol/L \times 4 Serum magnesium estimation Normal Range of Serum magnesium is 1.3-2.5 mEq/L Methodology: Calmagite method Principle: Magnesium combines with Calmagite in an alkaline medium to form a red coloured complex. Interference of calcium and proteins is eliminated by the addition of specific chelating agents and detergents. Intensity of the colour formed is directly proportional to the amount of magnesium present in the sample. Procedure: Wavelength/filter: 510 nm (Hg 546 nm)/green Temperature: Room temperature Light path: 1 cm Calculations: Magnesium in mEq/L = (Abs.T/Abs.S) \times 2 SI conversion factor: 2 mEq/L = 1 mmol/L = 2.44 mg/dl

Method of statistical analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean \pm SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance, student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups

Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Student t test has been used to find the homogeneity of parameters on continuous scale and Chi-square/Fisher exact test has been used to find the homogeneity of samples on categorical scale.

Results

Table 1: Comparison of age distribution in case and control group

Age (years)	Controls		Cases	
	N	%	N	%
18-20	19	38	16	32
21-25	26	52	22	44
26-30	4	8	7	14
31-35	1	2	5	10
Total	50	100	50	100
Mean \pm SD	22.88 \pm 2.88		23.87 \pm 4.25	

A comparative clinical study (case-control study) with 50 patients (PIH) and 50 normal pregnant women is undertaken to study the serum calcium and serum magnesium the present study was well matched in age between both groups and

comparable with the mean age in study group 22.88 \pm 2.28 years, control group 23.87 \pm 4.25. Majority of patients are in 21–25-year group in both study (44%) and controls (52%).

Table 2: Comparison of mean BP in control and case group

BP (mm Hg)	Controls	Cases	P value
SBP (mm Hg)	114.86 \pm 8.22	150.34 \pm 9.91	<0.001
DBP (mm Hg)	74.66 \pm 6.14	100.40 \pm 9.21	<0.001

Mean systolic blood pressure in study group was 150.34 \pm 9.91 mmHg and in controls 114.86 \pm 8.22 mmHg. Mean diastolic blood pressure in study group was 100.40 \pm 9.21 mmHg and in controls 74.64 \pm 6.14 mmHg.

Table 3: Comparison of serum calcium and serum magnesium in two groups

Outcome Variables	Controls	Cases	P value
Serum calcium (mg/dl)	9.11 \pm 0.82 (7.80-12.00)	8.12 \pm 0.37 (7.20-9.00)	<0.001
Serum Mg (mEq/L)	2.08 \pm 0.46 (1.30-3.10)	1.79 \pm 0.70 (1.00-4.70)	0.012

The Table 3 shows the concentration of serum calcium in controls as 9.11 \pm 0.82 and in study group 8.12 \pm 0.37 mg/dl with P value <0.001. The serum magnesium levels in controls 2.08 \pm 0.46 and in study group was 1.79 \pm 0.70 mEq/L with P value 0.012. The serum calcium and magnesium

has significantly decreased in cases compared to controls.

Discussion

Haemorrhage, hypertensive disorders and sepsis are responsible for more than half of all maternal deaths worldwide. [15-17]

The impact of pre-eclampsia is greatest in developing countries where it accounts for 20 – 80% of the striking increase in maternal morbidity and mortality. [17] There are many similarities between the management of gestational hypertension and that of preeclampsia. Adverse pregnancy outcomes can occur as a result of gestational hypertension as well as pre-eclampsia and thus the former may not be a separate entity from preeclampsia. A rapid rise in blood pressure poses a danger to both, the mother and the foetus and as such should not be ignored only because proteinuria has not yet developed. [18,19] Dietary deficiency of calcium consequently reduces serum calcium levels and has been implicated as a cause of pre-eclampsia in some studies. This theory can be explained by the vasoconstrictive effect that is caused by reduced serum calcium levels. [20]

The mean serum concentration of calcium in normal pregnancy is 9.11 ± 0.82 mg/dl and in pregnancy induced hypertension is 8.12 ± 0.37 mg/dl. The mean serum calcium concentration in pregnancy induced hypertension patients is decreased as compared to normal pregnancy and this decrease is of high statistical significance with p value <0.001 . This study result was similar to the result of various other studies like Nasser O Malas et al., [21] Kanchanpan Sukonpan et al., [22] Chanvitya Punthumapol MD et al., [23] Idogun ES et al., [24] Jain S et al. [25]

A tendency to relative maternal hypocalcaemia during pregnancy has been recognised for more than 40 years. Total calcium tends to decrease over the course of pregnancy in normal women and decreased significantly during pregnancy in women who developed preeclampsia. The decrease in serum calcium levels principally involves the protein bound portion and haemodilution. Belzian and associates 1983 noted decreased calcium levels in preeclampsia and achieved

decrease in blood pressure with calcium supplementation. [26,27]

In this study serum concentration of magnesium in normal pregnancy and pregnancy induced hypertension is 2.08 ± 0.46 mEq/L and 1.79 ± 0.70 mEq/L respectively. The mean serum magnesium concentration is decreased in preeclampsia compared to normal pregnancy. The P value is 0.013 which is of moderate significance. The present study results are comparable to study reports of K. Srivastava et al., [28] Kisters et al. [29]

An increase in renal clearance during pregnancy, poor dietary intake, consumption of minerals by growing fetal skeletal system, hemodilution, all contribute to hypomagnesaemia. In this study hypomagnesaemia has not been encountered in controls but a significant number of preeclampsia patients showed a tendency towards hypomagnesaemia. [30] The cause effect pattern is to be analyzed. Some studies like Sanders GT et al. 1999 have shown that serum magnesium was even higher in pre-eclamptic group than in normal pregnancy. The difference may be explained by the variation of the studied population and the dietary intake. [14]

Conclusion

The study data supported the hypothesis that calcium and magnesium deficiency might be the cause in the development of preeclampsia. The consequence of the deficiencies of the calcium and magnesium may be responsible for the clinical manifestations that are observed in preeclampsia and eclampsia patients since both ions are important in cellular and neuronal metabolism as well as cell membrane stability. Though calcium and magnesium deficiencies cannot be pin pointed as the sole factors in the etiology of PIH, these findings do support the hypothesis that hypocalcaemia and hypomagnesaemia could be possible modifiable factors in the causation of

hypertension in pregnancy and their relationship cannot be denied.

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