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RESEARCH ARTICLE

A COMPARATIVE STUDY BETWEEN SERUM MAGNESIUM AND CALCIUM LEVELS IN PRE ECLAMPSIA VERSUS NORMOTENSIVE PATIENTS

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Abstract

Preeclampsia is one of the most common causes of maternal and fetal morbidity and mortality. It is a recognised health challenge with devastating fetomaternal consequences. Nutritional deficiencies are commonly found in pregnant women and it is well established that the pregnant women from developing countries usually consume diets that are low in minerals and vitamins. Since the pathogenesis of preeclampsia has not been fully elucidated, the search for predictive markers and preventive strategies remains an unfulfilled issue. The study was conducted in the department of obstetrics and gynecology at Pravara Rural Hospital, Loni, Maharashtra, India to assess serum levels of calcium and magnesium in pregnant females who suffered from preeclampsia in comparison with normal pregnant ladies.

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Introduction:-

Preeclampsia (PE) is an idiopathic multisystem disorder specific to human pregnancy and is defined as the onset of hypertension and the presence of proteinuria during pregnancy, usually occurring after the 20th week of gestation in a previously normotensive woman and resolving completely by the sixth week after delivery of fetus.

Preeclampsia is one of the most common causes of maternal and fetal morbidity and mortality. It is a recognised health challenge with devastating fetomaternal consequences. It is the third most common cause of maternal death worldwide. Incidence of preeclampsia has been estimated at 5–14% pregnancies worldwide, 4–18% in developing countries with an increasing trend and accounts for about 20-80% of the maternal mortality in developing countries.

Despite prevalence and severity of preeclampsia, the pathophysiology of this multisystem disorder is still poorly understood. The pathophysiological mechanism involved is characterized with the failure of the trophoblastic invasion of spiral arteries which may be associated with increased vascular resistance of uterine arteries and decreased perfusion of the placenta. This may lead to the release of antiangiogenic factors into the maternal circulation and alter maternal systemic endothelial function to cause hypertension and other manifestations of the disease.

Nutritional deficiencies are commonly found in pregnant women and it is well established that the pregnant women from developing countries usually consume diets that are low in minerals and vitamins. Since the pathogenesis of preeclampsia has not been fully elucidated, the search for predictive markers and preventive strategies remains an unfulfilled issue (1). Recently calcium and magnesium levels have been implicated in the pathogenesis of PE.

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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. Calcium causes vasoconstriction by decreasing prostacyclin production and by increasing the vasoconstriction effect of angiotensin II and noradrenaline in the blood vessel wall (2). The lowering of serum calcium and the increase of intracellular calcium can cause an elevation of blood pressure in preeclamptic mothers so the modification of calcium metabolism during pregnancy could be one of the causes of pre-eclampsia.

Hypomagnesaemia in most pregnant women is associated with haemodilution, renal clearance and 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 PE. Magnesium levels may have significant effects on cardiac excitability and on vascular tone, contractility and reactivity. Magnesium causes vascular muscle relaxation(3). Pregnancy induced hypertension is characterized by vasospasm, elevated blood pressure and increased neuromuscular irritability, features common to syndromes of magnesium deficiency(4). Observational studies from medical records reported that magnesium supplementation during pregnancy was associated with reduced risk of preeclampsia(5).

Aim:-

This study aimed to assess serum levels of calcium and magnesium in pregnant females who suffered from pre-eclampsia in comparison with normal pregnant ladies.

Design and Study Method:-

The study was conducted in the department of obstetrics and gynecology at Pravara Rural Hospital, Loni, Maharashtra.

Study population comprised pregnant women admitted in the hospital between January 2023 and March 2023.

This study is a case control study. The study constituted 120 members, between 32 and 40 weeks of gestation, which included 60 pre-eclamptic women and 60 normotensive women.

Inclusion Criteria- Cases

The patients were included in the case group were singleton pregnancy and between age of 18 to 40 years.

1. Pre-eclampsia was diagnosed based on standard criteria, where in blood pressure $\geq 140/90$ mmHg on 2 separate occasions 6 hours apart and proteinuria with or without end-organ involvement.
2. Proteinuria $\geq +1$ on dipstick or ≥ 300 mg per 24 hrs urine collection

Inclusion Criteria-Controls

The control group included singleton pregnancy with more than 32 weeks gestational age between age 18 to 40 years.

Exclusion Criteria

The patients with multiple pregnancy, chronic hypertension, gestational diabetes mellitus, renal or cardiovascular disease, thyroid disorder and anaemia were excluded from the study.

An approval of the study protocol was obtained from the ethical committee prior to the commencement of the study. 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, obstetric examination). Written informed consent was obtained from each woman before inclusion in the study. A standard interview-based questionnaire was used to obtain data on demography, clinical and family history. Gestational age was determined based on last menstrual period and confirmed by first trimester scan.

Serum calcium levels were estimated by Roche kit by 5-nitro-5'-methyl BAPTA method. Serum magnesium was estimated by Roche kit by Xylidyl blue method.

Univariate and bivariate analysis were performed to assess the differences in demographic, anthropometric and biochemical parameters. Descriptive means, standard deviations and/or distributions were generated for all study

variables. Pearson's correlation was used to study the correlation among the study parameters. Results were summarized in a comparison table of mean serum calcium and magnesium levels in women from the 2 groups using p-values and independent t-tests.

Statistical analysis:

A p-value <0.05 was considered statistically significant. The data was analysed using SPSS statistical software (version 20.0).

Results:-

A total 120 pregnant women of gestational age ranging from 32 to 40 weeks of gestation were recruited for the study. Out of them, 60 women were normotensive who comprised the control group. 60 women were pre-eclamptic, comprising the study group. Serum calcium and magnesium levels were analysed for all the women.

75% of pre eclamptic women and 70% of normotensive women were primigravida.

The mean age of control group was 24.6±4.28 years whereas mean age of study group was 24.316±4.43 years. p-value was 0.156 which is statistically insignificant.

Out of the total 60 pre-eclamptic women, 44 (73.3%) had mild pre-eclampsia while 16 (26.7%) had severe pre-eclampsia. In the pre-eclamptic group, 20 (33.3%) patients had no proteinuria, 23 (38.33%) of pre-eclamptic women had urine albumin +1, 10 (16.66%) had urine albumin +2 while 7 (11.66%) had urine albumin \geq +3. Majority (65%) of the patients developed pre-eclampsia at 32-34 weeks of gestation. 28 (46.7%) of women who had pre-eclampsia required no treatment and were managed on close observation. 26 (43.3%) were started on antihypertensive drugs to manage their condition. 6 (10%) had to be given magnesium sulphate along with antihypertensive drugs, either for prophylactic or therapeutic purposes. Among the patients who had pre-eclampsia, 4 (6.7%) developed placental abruption, while 1 (1.7%) developed eclampsia.

GROUP	SAMPLE SIZE	MEAN	STANDARD DEVIATION
CONTROL	60	1.9245	0.44659
STUDY	60	1.7042	0.40623

Comparison Of Serum Magnesium Levels Between Pre-Eclamptic And Normotensive Women p value is 0.001

Degree of pre-eclampsia	N	MEAN	STANDARD DEVIATION
NORMAL	60	1.9245	0.44659
MILD	44	1.7716	0.42166
SEVERE	16	1.5925	0.37432
TOTAL	120	1.8517	0.42791

Relationship Between Serum Magnesium Levels And Degrees Of Pre-Eclampsia p value is 0.001

GROUP	N	MEAN	STANDARD DEVIATION
CONTROL	60	10.2837	1.18067
STUDY	60	9.4567	1.14522

Comparison Of Serum Calcium In Normotensive And Pre-Eclamptic Patientsp value is 0.004

Degree of pre-eclampsia	N	MEAN	STANDARD DEVIATION
NORMAL	60	10.2837	1.18067
MILD	44	9.4991	1.14562
SEVERE	16	9.3588	1.24807
TOTAL	120	9.7907	1.25785

Relationship Between Serum Calcium And Degrees Of Pre-Eclampsia p value is 0.014

PARAMETERS	CALCIUM		MAGNESIUM	
	r value	p value	r value	p value
SYSTOLIC BP	-0.629	<0.001	-0.554	<0.001
DIASTOLIC BP	-0.653	<0.001	-0.553	<0.001
PROTEINURIA	-0.652	<0.001	-0.482	<0.001

Serum calcium and magnesium showed a negative correlation to systolic bp, diastolic bp and proteinuria.

Discussion:-

The mean serum magnesium level in the control group in the study was 1.9245 ± 0.446 mg/dl.

In the study group, mean serum magnesium level was 1.7042 ± 0.406 mg/dl. p-value was 0.001, which is significant, indicating that serum magnesium levels are significantly lower in women who develop pre-eclampsia as compared to normotensive pregnant women.

Ugwuja et al, conducted a study in Nigeria in 2016 which had the same result(6). Similar results were obtained by Bandeduche S et al in a study where they concluded that serum magnesium levels are significantly decreased ($p < 0.001$) in women of pre-eclampsia as compared to normal pregnant women(7). However, Darkwa et al, found no significant difference in the mean serum levels of magnesium between pre-eclamptic and normal pregnant women in a study conducted in 2017 in Ghana(8).

Further, it was also seen in the study that mean serum magnesium level in mild pre-eclampsia was 1.771 ± 0.421 mg/dl, while in severe pre-eclampsia was 1.592 ± 0.374 mg/dl. p-value is 0.001. So, there is a significant relationship between serum magnesium levels and degree of pre-eclampsia. Serum magnesium level is lower in severe pre-eclampsia than in mild pre-eclampsia. Similar findings were reported by Deshpande et al in a study conducted in D. Y. Patil Hospital in 2018(9). They reported that severe cases of pre-eclampsia had lower mean value of serum magnesium compared to mild cases. Moholkar et al came to a similar conclusion in a study conducted in Government Medical College, Miraj during 2008-2010(10). In the present study, it is found that mean serum calcium level in the control group was 10.283 ± 1.27 mg/dl while mean serum calcium level in the study group was 9.461 ± 1.164 . p-value is 0.004, which is statistically significant. So, it can be concluded from this study that serum calcium levels are significantly lower in pre-eclampsia patients compared to normotensive pregnant women.

However, Roy HL et al in their study found that the mean serum calcium did not differ significantly between the subjects of pre-eclampsia and normal pregnant women ($p=0.963$)(11). This was in contrast with several studies suggesting hypocalcaemia as a possible cause of pre-eclampsia. For example, Onyegbule OA et al conducted a study in 2014 in Nigeria and found that there is significant reduction in the level of serum calcium in pre-eclamptic women as compared to normotensive women ($p<0.001$). They suggested dietary supplementation or direct replacement therapy of calcium for women with pre-eclampsia(12). Their study supported the hypothesis that calcium deficiency might be one of the causes in the development of pre-eclampsia.

Further, it was seen that, mean serum calcium level in mild pre-eclampsia was 9.499 ± 1.145 mg/dl, while in severe pre-eclampsia was 9.358 ± 1.248 mg/dl. p -value is 0.014. So, it is seen that there is a significant relationship between serum calcium level and degree of pre-eclampsia. Hence it can be concluded that serum calcium level is lower in severe pre-eclampsia than in mild pre-eclampsia. Deshpande et al, also found similar results in their study done in 2018. They selected a total number of 256 cases in the third trimester of pregnancy and divided into study and control groups of 128 each. The 128 cases in the study group were further divided into 3 sub-groups-mild, moderate and severe based on their blood pressure readings. They found that though there was no specific decreasing trend observed with increase in the intensity of pre-eclampsia, the mean levels of serum calcium of all 3 sub-groups were towards the lower side, more so in the sub-group of severe cases. However, in a study conducted by Vafae et al, in Iran in 2014, it was found that the severity of pre-eclampsia was not influenced by the serum level of calcium.

Conclusion:-

Both serum calcium and serum magnesium in preeclamptic pregnant women were lesser in comparison to their healthy pregnant counterparts. These outcomes support the postulation that there is a cause- consequence liaison between hypocalcaemia and hypomagnesaemia as potential etiologic factors incriminated in of preeclampsia pathogenesis.

Therefore, based on this study, serial measurements of serum ionic calcium and magnesium among women who are at risk of PE may be used to predict the onset and severity of PE. However, therapeutic intervention to supplement calcium and magnesium in pregnant women for prevention of PE requires further study.

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