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Correlation of Serum Calcium and Magnesium with Preeclampsia

Sadia Haleema[1], Muhammad Imran[2] and Javaria Zafar[2]
[1]*Department of Biochemistry, Continental Medical College, Lahore*
[2]*Department of Physiology, Continental Medical College, Lahore*

ABSTRACT

Introduction: Preeclampsia is a common complication during pregnancy and affects both mother and the outcome of pregnancy. The pathophysiology of Preeclampsia is yet to be understood but there is evidence that altered ionic balance of calcium and magnesium may play a role in development of raised arterial pressure in this disease. **Aims and Objectives:** The current study was aimed to observe correlation between serum calcium and magnesium levels with arterial pressure in pregnant women. **Place and Duration of study:** This study was carried out in 2012, in the Department of Biochemistry and Chemical pathology, Shaikh Zayed Hospital, Lahore. **Material and Methods:** In this cross-sectional analytical study, 121 pregnant women in their first trimester of pregnancy were recruited. Their serum Ca^{+2} and Mg^{+2} levels and arterial pressures were measured at different time interval (ie. at 18th, 24th and 35th week) of pregnancy. Data obtained was summarized and entered into SPSS. Statistical tests were applied for comparison and correlation between different groups of the data. **Results:** After 20th week of gestation, 35 women were found to have low calcium and magnesium levels and developed Preeclampsia whereas 86 remained normal. Mean serum Ca^{+2} and Mg^{+2} levels were significantly lower in preeclamptic group than those of normal pregnant women. Serum Ca^{+2} and Mg^{+2} levels showed significant negative correlation with arterial pressure in preeclamptic women. **Conclusion:** It was concluded that serum calcium and magnesium levels are correlated with arterial pressure and their deficiency may be a risk factor for development of Preeclampsia.

Keywords: Calcium, Magnesium, Arterial pressure, Preeclampsia.

INTRODUCTION

The definition of hypertension in pregnancy is arterial pressure ≥140/90mmHg recorded a minimum of two different occasions which are at least 6 hours apart. Preeclampsia is the development of hypertension and proteinuria after twentieth week of pregnancy, in an otherwise normal woman and recovering completely by the 6th week after parturition. Approximately 10% of all pregnancies are complicated by hypertension worldwide and preeclampsia is an important factor for morbidity mortality in such patients during and after pregnancy[1]. According to a research, Preeclampsia affects 3-9% of gestations and a total of 11-16% of deaths are related with preeclampsia[1]. The pathophysiology of preeclampsia may involve raised vascular resistance in uterine artery and low placental perfusion, in the face of inflammatory condition, which accompanies pregnancy. This inflammation provokes vascular and circulatory changes. Studies have shown that acute atherosis and the associated thrombosis are the cause of infarctions which occur in placenta.[2] Gestational hypertension and preeclampsia are considered either two different conditions affecting the same organs or variable severity of the same disorder.[3] WHO reports that every year up to 40 thousand women die of hypertensive disorders, mostly in developing countries[4]. Unfortunately mortality rate in Pakistan is high where 1 out of 89 females succumb to maternal causes, with preeclampsia being major factors[5]. The studies have shown a strong

correlation of Ca^{+2} and Mg^{+2} with preeclampsia. Generally adults absorb only 20% of Ca^{+2} in their daily diet. The pregnant women increase this absorption level of Ca^{+2} to 60% in the 2nd trimester and 70% in the 3rd trimester.[6] It has been proven that inverse association exists between Ca^{+2} intake and development of hypertension during pregnancy.[7] During development, as the fetal skeleton forms, more Ca^{+2} is utilized in forming the bones. To meet these requirements, the mother's Ca^{+2} absorption rate from gut increases, mainly in the last two trimesters. But in preeclampsia, these compensatory changes do not function adequately or function abnormally. The Ca^{+2} supplements in pregnancy cause a fall in gestational hypertension, although the effect depends upon the daily dietary Ca^{+2} intake of women and pre-existing risk factors. They also reduce hypertension in pregnancy by decreasing smooth muscle contractility and causing vasodilation.[7] It is also known that Mg^{+2} is an essential element and is important in cardiovascular function. Hypomagnesaemia may be due to an increase in the renal excretion during pregnancy. Mg^{+2} deficiency may cause hypertension, as there is negative correlation between serum Mg^{+2} levels and blood pressure.[7] Magnesium has role in regulation of proteins related to contraction, transport across membrane of calcium, sodium etc, and works as a cofactor in ATPase activity.[8] Also Mg^{+2} influences vascular tone by release of EDRF, cyclooxygenase derived prostanoids.[8] $MgSO_4$ is used for treatment of seizures and prophylaxis of eclampsia and preeclampsia.[8] Although the natural homeostatic mechanisms tend to maintain Ca^{+2} and Mg^{+2} level, but lower levels of these ions in women with preeclampsia may indicate the dietary deficiency of micronutrient which can be an important factor for the occurrence of the hypertensive disease in pregnant women. The current study is aimed to observe alterations in serum calcium and magnesium levels during different time intervals of pregnancy and correlate them with arterial pressure.

MATERIAL AND METHODS

This was a cross sectional analytical study, carried out in the Department of Biochemistry and Chemical Pathology, Shaikh Zayed Hospital, Lahore (SZHL), during 2012. The study was conducted after approval from Institutional Review Board (IRB) of SZHL. A total of 121 subjects were selected. The sample size was calculated at the confidence level of 95% with an alpha of 0.05. Inclusion criteria were the pregnant women in the first trimester of their pregnancy who gave consent to be a part of the study. Exclusion criteria were hypertension prior to pregnancy, diabetes, and renal, hepatic, cardiac or any other systemic diseases. The subjects were recruited from the antenatal clinic of SZHL. After obtaining relevant history, the height and weight of the pregnant women was measured using standard scales. The body mass index (BMI) in kg/m^2 was then calculated and blood pressure of the women was measured. The demographic information, history and examination findings were recorded on the prescribed proforma. Blood samples of each patient were taken at three different intervals of pregnancy for the analysis of serum Ca^{+2} and Mg^{+2} levels. First sample was taken at 18th week, 2nd sample was taken at 24th week and 3rd sample was taken at 35th week of gestation. A 3 mL of venous sample from each subject was drawn. A 1.5 mL aliquot was taken in plain tube, allowed to clot for 20-30 minutes and then centrifuged. Serum thus obtained was preserved in labelled eppendorf tubes at -20ºC for the estimation of serum Ca^{+2} and Mg^{+2}. The biochemical tests for Ca^{+2} and Mg^{+2} were performed on the serum samples, by auto analyzer machine.

Statistical Analysis:

Computer software SPSS (version 21) was used to conduct the statistical analysis. Results of Ca^{+2} and Mg^{+2} levels were expressed as mean ± SD. Student t-test was used for comparison between preeclamptic and non-preeclamptic pregnant women. ANOVA was used for comparing levels of Ca^{+2} and Mg^{+2} at different time intervals of pregnancy. The correlation between serum Ca^{+2} and Mg^{+2} with arterial pressure at different time intervals of pregnancy was determined using Pearson correlation coefficient 'r'. A p-value of less than 0.05 was considered statistically significant.

RESULTS

We recruited 121 pregnant women, and obtained their complete history and performed clinical examination. The comparison of age, height, weight and BMI in three time intervals in pregnant women was performed. There was no significant difference between the mean ages, weight, height

and BMI among the pregnant women. The comparison of serum Ca^{+2} and Mg^{+2} levels and mean systolic arterial pressure, was done at three different time intervals of pregnancy. Out of 121 pregnant women, 35 women had significantly low calcium and magnesium levels as compared to normal. These women developed preeclampsia after 20th week of pregnancy.

Status of pregnant women	Frequency	%age
Non-preeclamptic	86	71.07
Preeclamptic	35	28.92
Total	121	100.0

Table-1: The frequency of non-preeclamptic and preeclamptic pregnant women

Mean Ca^{+2} level in non-preeclamptic women was 9.70 ± 0.16 mg/dl. Although it was not significantly different from that of preeclamptic women at 1st time interval (9.64 ± 0.25 mg/dl), but it was significantly higher ($p < 0.01$) in relation to that in preeclamptic women at 2nd time interval (7.70 ± 0.51 mg/dl) and at 3rd time interval (7.64 ± 0.29 mg/dl) of pregnancy. Comparison of mean serum Ca^{+2} between non-preeclamptic and preeclamptic women at different time intervals has been illustrated in figure-1.

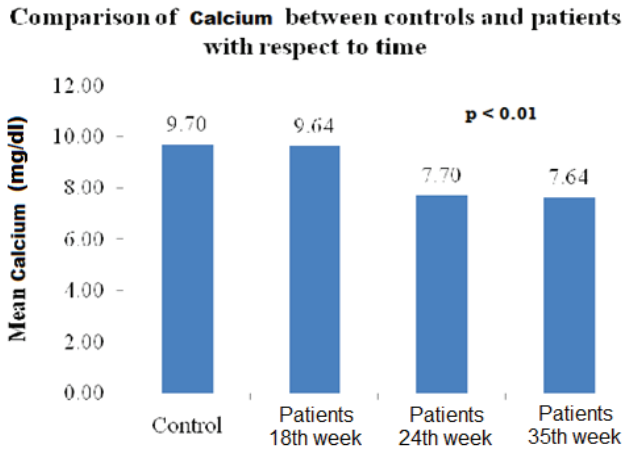

Figure-1: Comparison of serum Ca^{+2} level between non-preeclamptic and preeclamptic pregnant women with respect to different time intervals of pregnancy. ($p< 0.01$)

Mean Mg^{+2} level in non-preeclamptic women was 1.89 ± 0.14 mg/dl. Although it was not significantly different from that of preeclamptic women at 1st time interval (1.91 ± 0.02 mg/dl), but it was significantly higher ($p < 0.01$) in relation to that in preeclamptic women at 2nd time interval (1.74 ± 0.13 mg/dl) and at 3rd time interval (1.55 ±0.15 mg/dl) of pregnancy. Comparison of mean serum Mg^{+2} between non-preeclamptic and preeclamptic women at different time intervals has been illustrated in Figure-2.

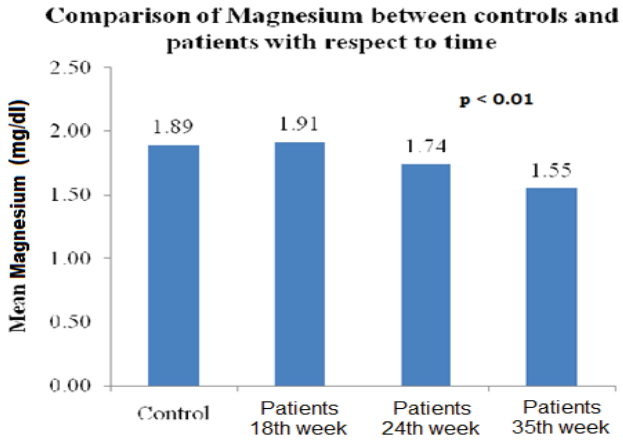

Figure-2: Comparison of serum Mg^{+2} level between non-preeclamptic and preeclamptic pregnant women with respect to different time intervals of pregnancy. ($p< 0.01$)

There was strong negative correlation between serum calcium and systolic arterial pressure during 2nd and 3rd time interval of pregnancy among preeclamptic patients (r -0.78 and -0.81 respectively). Also, there was strong negative correlation between serum magnesium and systolic arterial pressure during 2nd and 3rd time interval of pregnancy among preeclamptic patients (r -0.68 and -0.70 respectively). The correlation of systolic arterial pressure with calcium and magnesium level, at 2nd and 3rd time interval of pregnancy is shown in Table-2.

Interval	Mean systolic arterial pressure	Serum calcium level	Pearson correlation 'r'	Mean systolic arterial pressure	Serum magnesium level	Pearson correlation 'r'
2nd time interval (24th week)	142. 34 mmHg	7.70±0.51 mg/dl	**-0.78**	142. 34 mmHg	1.74±0.13 mg/dl	**-0.68**
3rd time interval (35th week)	153. 27 mmHg	7.64±0.29 mg/dl	**-0.81**	153. 27 mmHg	1.55±0.15 mg/dl	**-0.70**

Table-2: Correlation of systolic arterial pressure with calcium and magnesium level, at 2nd and 3rd time interval of pregnancy

DISCUSSION

The study was carried out aiming at evaluating the role of magnesium and calcium during development of preeclampsia. The mean serum $Ca^{+2}$and Mg^{+2} level in preeclamptic at 24th week was lower in comparison to non preeclamptic. Likewise a highly significant difference ($p < 0.001$) was observed when mean serum $Ca^{+2}$and Mg^{+2} level of preeclamptic women were compared with non preeclamptic women at 35th week of gestation. These findings were compatible with the study conducted by Al-Rubaye et. al.[7] They showed a significant reduction in serum Ca^{+2} and Mg^{+2} levels throughout the course of pregnancy whether among preeclamptic or normal pregnant women. In a study conducted in Nigeria, Adewolu revealed no correlation between serum $Ca^{+2}$and preeclampsia and concluded that Ca^{+2} may not cause preeclampsia among the study subjects. The statistical analysis of current study shows that there is no significant correlation between the age, weight, height and BMI of the non preeclamptic and preeclamptic group was observed. These results are in accordance with those reported in the literature.[9] However some studies show higher BMI ($p<0.001$) in preeclamptic as compared to non preeclamptic.[10]The difference of serum Ca^{+2} in non preeclamptic and preeclamptic at 18th week was insignificant. Besides mean serum Ca^{+2} in preeclamptic was lower in comparison to non preeclamptic during at 24th week and 35th week of gestation. These findings are consistent with many previous studies reported in the literature.[7,9,10] In the current study mean serum Ca^{+2} level in preeclamptic women at 24th week was 7.70 ± 0.51 mg/dl and at 35th week of gestation was 7.64±0.29 mg/dl. This may suggest poor dietary intake of calcium by the pregnant women. A study conducted in 2013 on preeclamptic women in Karachi showed that the level of serum calcium and serum magnesium was significantly lower in preeclamptic women than in normal healthy controls. In their study serum calcium was 7.02 ± 0.99 mg/dl in preeclamptic patients as compared to 9.34 ± 0.57 mg/dl in normal women. Similarly serum magnesium was 1.3 ± 0.34 mg/dl in preeclamptic patients as compared to 1.88 ± 0.16 mg/dl in normal women.[11] A Study from Coastal India showed that serum calcium concentration was significantly lower in the preeclamptic group compared to normotensives (7.84 ± 0.87 mg/dl vs 8.97± 0.69 mg/dl, $p<0.01$) whereas the levels of serum magnesium showed a marginal difference in both the groups (1.43± 0.55 mg/dl vs, 1.57 ± 0.72 mg/dl; $p = 0.257$).[12] In another study, women with preeclampsia had significantly lower serum calcium and magnesium levels than those in the control group ($p < 0.01$).[13] A similar study was conducted in the year 2011 in Pakistan at Agha Khan University, Karachi, by Amir Imdad and co-workers. Data from 10 clinically randomized trials on non-preeclamptic women carried out in developing countries, was described. Close analysis showed that Ca^{+2} supplements during gestational period were correlated with decrease in the risk of gestational hypertension in 45% and reduction in the risk of preeclampsia in 59% patients.[14] A case-control study in Riyadh, Saudi Arabia showed that mean values of calcium and magnesium were 7.78 ± 0.44 mg/dl and 1.54 ± 0.14 mg/dl respectively in the high risk group.[15] Another study by Aruna Patel et al showed that serum Ca^{+2} levels in normal pregnant women was 9.8 mg/dl and in mild preeclamptic women it was 8.74 mg/dl and in severe preeclamptic women, it was 8 mg/dl.[16] In a study conducted in Guatemala in 1980, researchers described negative correlation between calcium intake and hypertension of pregnancy.[17] In another study Mahomed et al., described a decreased intake of Ca^{+2}in numerous countries of the world during pregnancy, including western countries.[18] Ugwuja reported a possible role for magnesium but not calcium in the pathogenesis of preeclampsia, with overweight BMI in normal pregnant women.[19] The study conducted by Elmugabil et al also showed significant correlation between preeclampsia and serum levels of calcium and magnesium.[20] Pairu, in his recent work, concluded that the serum calcium and magnesium levels are decreased in pregnancy-induced hypertension compared to normal pregnant women, suggesting the possible role of calcium and magnesium in pathophysiology of pregnancy-induced hypertension.[21] It is to be noted that in the current study, there were certain important limitations due to financial and time constraints. Moreover, it was a single centered study with a relatively smaller sample size. A follow up prospective study of longer duration and larger sample size should be carried out in future.

CONCLUSION

Our study showed that serum calcium and magnesium levels are correlated with arterial pressure and the deficiency of calcium and magnesium may be a risk factor for development of high arterial pressure and preeclampsia in pregnant women. This study emphasizes the need of monitoring these electrolytes during antenatal period and appropriate measures such as addition of dietary supplements may decrease the incidence of preeclampsia. The results may also alert the obstetrician to harmful effects of these deficiencies on obstetric outcome.

REFERENCES

1. Duley L. The Global Impact of Preeclampsia and Eclampsia. Seminars in Perinatology 2009; 33:130-7.
2. James D.K, Weiner C.P, Steer P.J. High Risk Pregnancy: Management Options. 3rd ed. India: Elsevier; 2006; p.773-4.
3. Villar J, Carroli G, Wojdyla D, Abalos E, Giordano D, Ba'aqeel H, et al. Preeclampsia, gestational hypertension and intrauterine growth restriction, related or independent conditions. Am. J. Obstet. Gynecol, 2006; 194: 921-31.
4. Viller J, Say L, Shennan A, Linheimer M, Duley L, Conde-Agudelo A, et al. Methodological and Technical issues related to the diagnosis, screening, prevention and treatment of Preeclampsia and eclampsia. Int. J. Obstet. Gynecol, 2004; 85 Suppl 1:28-41.
5. Khan KS, Wojdyla D, Say L, Gulmezoglu Am, Van Look PFA. WHO Analysis of causes of maternal death: a systemic review. The Lancet 2006; 367: 1066-74.
6. Mudy G.R, Guise T.A. Hormonal Non-preeclamptic of Ca^{+2} Homeostasis. The American Association for Clinical Chemistry; 1999.
7. Al-Rubaye F.G, Al-Bayati M.M, Al-Khayat T.H. Mineral Homeostasis in Preeclampsia. Iraqi Journal of Medical Sciences 2009; 7(2):4-11.
8. Sontia B, Toyz R.M. Role of Mg^{+2} in Hypertension. Archives of Biochemistry and Biophysics 2006; 1-7.
9. Punthumapol C, Kittichotpanich B. Serum Ca^{+2}, Mg^{+2} and Uric Acid in Preeclampsia and Normal Pregnancy. J Med Assoc Thai 2008; 91:968-73.
10. Akhtar S, Begum S, Ferdousi S: Calcium and zinc deficiency in pre-eclamptic women. J Bangladesh Soc Physiol 2011, 6(2):94–99
11. Aziz R, Mahboob T: Serum Calcium, Magnesium and Parathyroid Hormone in Normal Pregnant and Pre-eclamptic Women in Karachi, Pakistan. J Hypertens 2014, 3:143.
12. Kanagal DV, Rajesh A, Rao K, et al. Levels of Serum Calcium and Magnesium in Pre-eclamptic and Normal Pregnancy: A Study from Coastal India. *Journal of Clinical and Diagnostic Research : JCDR*. 2014; 8(7)
13. Ephraim RKD, Osakunor DNM, Denkyira SW, Eshun H, Amoah S, Anto EO. Serum calcium and magnesium levels in women presenting with Preeclampsia and pregnancy-induced hypertension: a case–control study in the Cape Coast metropolis, Ghana. *BMC Pregnancy and Childbirth*. 2014; 14:390
14. Imdad A, Jabeen A, Bhutta Z.A. Role of Ca^{+2} supplementation during pregnancy in reducing risk of developing gestational hypertensive disorders, a meta-analysis of studies from developing countries. BMC Public Health 2011; 11:18
15. Noura Al-Jameil, Hajera Tabassum, Mir Naiman Ali, Mohammed Abdul Qadeer, Farah Aziz Khan, May Al-Rashed: Correlation between serum trace elements and risk of Preeclampsia: A case controlled study in Riyadh, Saudi Arabia. Saudi J of Biol. Sci.: Vol 24 (6), 2017, 1142-48
16. Patel A, Singh B, Patel A, Sharma M. Serum Ca^{+2} level in pregnancy induced hypertension. Int J Biol Med Res. 2012: (3), 1914-1918.
17. Belizan JM, Villar J. The relationship between calcium intake and oedema, proteinuria and hypertension gestosis: a hypothesis. Am J Clin Nutr. 1980; 33:2202–10
18. Mahomed K, Williams MA, Woelk GB, Mudzamiri S, Madzime S, King IB, et al. Leukocyte Selenium, Zinc, and Copper Concentrations in Pre-eclamptic and Normotensive Pregnant Women. Biol Trace Elem Res. 2000; 75:107–18
19. Ugwuja EI, Famurewa AC, Ikaraoha CI: Comparison of Serum Calcium and Magnesium Between Preeclamptic and Normotensive Pregnant Nigerian Women in Abakaliki,

Nigeria.Ann Med Health Sci Res. 2016; 6(1): 33–37.
20. Elmugabil A, Hamdan HZ, Elsheikh AE, Rayis DA, Adam I, Gasim GI: Serum Calcium, Magnesium, Zinc and Copper Levels in Sudanese Women with Preeclampsia. PLoS ONE 2016, 11(12).
21. Pairu J, Triveni GS, Manohar A: The study of serum calcium and serum magnesium in pregnancy induced hypertension and normal pregnancy. Int J Reprod Contracept Obstet Gynecol. 2015; 4(1):30-34

The Authors:

Dr. Sadia Haleema
Assistant Professor
Department of Biochemistry,
Continental Medical College, Lahore.

Dr. Muhammad Imran
Associate Professor
Department of Physiology,
Continental Medical College, Lahore.

Dr. Javaria Zafar
Demonstrator
Department of Physiology,
Continental Medical College, Lahore.

Corresponding author:

Dr. Muhammad Imran
Associate Professor
Department of Physiology,
Continental Medical College, Lahore.
dr.imran.ap@gmail.com