

Effects of the Serum Calcium and Magnesium Level in the Development and Complications of Pregnancy Induced Hypertension; A Case-control Study among Sample of Iraqi Pregnant Women, 2022

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Abstract

Background: Preeclampsia is a systemic disease characterized by hypertension, proteinuria and edema, which are thought to be the result of diffuse endothelial activation and dysfunction.

Aim: This study aims to provide preliminary data that could influence the prevention and management of PIH.

Patients and Methods: A case-control study conducted in Salahadeen General Hospital /Gynecology and Obstetrics department during the period from 1st of January to 30th of June 2022. A convenient sample of 100 singleton pregnant women with a live fetus and gestational age of 20 weeks or more were enrolled (50 pregnant women with preeclampsia or eclampsia and 50 pregnant women in good health as control group. Twenty-four-hour automatic blood pressure monitoring was performed and blood was collected for determination of Serum Calcium and Magnesium by Conventional laboratories procedure and manufactures instructions.

Results: There was not a significant difference between the studied cases and the control group in terms of patient age, gestational age at the time of sampling, or parity ($P>0.05$). On the other hand, there was a significant difference between the studied cases and the control group in terms of systolic and diastolic blood pressure ($P<0.05$). The study demonstrated that Serum calcium mean was significantly decreased in pregnant women with preeclampsia (8.17 mg/dl) as compared with the control group (9.43 mg/dl) (P . value <0.01). The study demonstrated that Serum Magnesium mean was significantly reduced in pregnant women with Pre-eclampsia (1.73 mEq/L) as compared with the control group (2.15 mEq/L) (P . value <0.01). The study demonstrated that Serum calcium and Magnesium mean were significantly decreased in pregnant women with severe preeclampsia (8.01 mg/dl) as compared with the mild preeclampsia (9.43 mg/dl) (P . value <0.01).

Conclusions: The study demonstrated that Serum calcium and magnesium significantly decreased in pregnant women with preeclampsia especially in severe preeclampsia. Nutritional health education should be used as a preventive approach to allow the large sector of the developing countries population to maximize the use of the limited resources in the best way.

Keywords: Serum Calcium, Magnesium, Pregnancy, Induced Hypertension, Preeclampsia.

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INTRODUCTION

Preeclampsia (PE), as a risky pregnancy, is a systemic disease characterized by hypertension, proteinuria and edema, which are thought to be the result of diffuse endothelial activation and dysfunction⁽¹⁾. About 5% of all pregnant women have PE during the second half of gestation that can cause maternal death throughout the world and is accompanied by substantial perinatal morbidity and mortality. Pregnancy-induced hypertension (PIH) is a new onset of hypertension that appears at 20 weeks or more gestational age of pregnancy with or without proteinuria. This umbrella definition includes gestational hypertension, preeclampsia (when the

hypertension is associated with proteinuria ≥ 30 mg/day or, if not available, a protein concentration ≥ 30 mg ($\geq 1+$ on dipstick) in a minimum of two random urine samples collected at least 4–6 hours), and eclampsia which is defined as a new onset of generalized tonic-clonic seizures in a woman with preeclampsia, it can occur antepartum, intrapartum, and postpartum^(2,3). Globally, PIH represents a significant public health threat contributing to high perinatal deaths, it complicates 2–8% of pregnancies in developed countries with increasing up to 16.7% in developing countries⁽¹⁾. The previous history of pre-eclampsia, pre-existing diabetes, multiple pregnancies, nulliparity, and advanced maternal age (≥ 40 years) have been reported to

increase the risk of PIH⁽⁴⁾. Current evidence suggests that the endothelial dysfunction seen in preeclamptic pregnant women may persist years after the episode, and therefore preeclamptic women may be at high risk of cardiovascular diseases later in life⁽⁵⁾. Though the etiology of preeclampsia remains unclear, many theories suggest abnormal placental implantation and abnormal trophoblastic invasion as possible causes. The molecular basis of this condition is unresolved in literature⁽⁶⁾. It has been postulated that fluctuations in maternal serum ions may be the precipitating cause of elevated blood pressures in preeclampsia⁽⁷⁾. Dietary deficiency of mineral ions has been shown to have a harmful effect on the pregnant mother and growing fetus and possibly complicate preeclampsia⁽⁸⁾. Dietary deficiency of magnesium has been established to play a role in blood pressure regulation and hence development of preeclampsia⁽⁹⁾. Evidence supporting routine magnesium supplementation for all pregnant women has not been substantiated by research, though most studies have reported reduced magnesium levels in pregnancy and worse levels in preeclampsia. However, other studies have also reported a nonsignificant change in the serum magnesium levels of preeclamptic women compared to normal pregnant women^(10,11). Various studies have also reported reduced serum calcium levels in preeclampsia compared to normal pregnant women. In addition, previous reports have considered the association between PIH and serum electrolytes, particularly (Ca²⁺) and magnesium (Mg²⁺), it has been reported that there are reduced levels of Ca²⁺ and Mg²⁺ in pre-eclampsia^(8,12,13). This study aims to provide preliminary data that could influence the prevention and management of PIH.

Patients and methods

A case-control study conducted in Salahadeen General Hospital /Gynecology and Obstetrics department during the period from 1st of January to 30th of June 2022. A convenient sample of 100 singleton pregnant women with a live fetus and gestational age of 20 weeks or more were enrolled. The sample consisted of 2 groups:

- **Preeclamptic group:** Include 50 pregnant women who met the criteria of preeclampsia or eclampsia.
- **Control group:** include 50 pregnant women in good health, normotensive, and without dipstick proteinuria.

Exclusion criteria

- Pregnant women with chronic hypertension, diabetes mellitus, chronic kidney disease, liver disease, cardiovascular disease, thyroid or other endocrine disorders, and malignancy.
- Pregnancies with major maternal or fetal abnormalities including hydatidiform mole, placenta accrete, and abrupt placenta.

- Pregnant women with a history of smoking or consumption of a drug that might affect their blood pressure.

Ethical approval

- Approval of the council of College of Medicine / Tikrit University was obtain for the proposal of the study.
- Approval permission was presented to the director of Salah Al-Din Health directorate / Salah Al-Din General Hospital.
- An interview was carried out with these patients using questionnaire form designed by the investigator including their demographic characteristics, age, weight, length. etc
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Data collection

- The data will be collected through a questionnaire that will be prepared by the researcher after a review of similar articles with revision by the supervisor. The questionnaire is divided into three parts.
- Part one: Sociodemographic characteristics, including age, employment, and residency.
- Part two: medical and obstetrical history and examination, including gestational age, parity, gravidity, abortions, number of cesarean sections (CS), mean of the interpregnancy period, history of contraceptive pill use, and body mass index, blood pressure measurement.
- Part three: The laboratory results of Ca²⁺ and Mg²⁺, and proteinuria.

METHODS

Twenty-four-hour automatic blood pressure monitoring was performed Blood pressure readings were taken at 30minute intervals. For patients who was admitted to the hospital, and two readings of blood pressure was taken for patients who was not admitted to the hospital and diagnosed as hypertensive disorders depend on history and examination and blood pressure readings that record on antenatal card in each antenatal visit. Measurement of Bp done by sphygmomanometer in sitting position, with cuff size appropriate to patients arm circumference was used and to eliminate a possible stressor for the patients, the visual preview of blood pressure measurement was removed. Mild preeclampsia is defined as a blood pressure of at least 140/90 mmHg measured on two occasions each 6 hours apart, accompanied by proteinuria of at least 300 mg per 24 hours, or at least 1+ on dipstick testing. Severe preeclampsia is defined as having one or more of the following criteria: blood pressure of at least 160/110 mmHg measured on two occasions each 6 hours apart, proteinuria of at least 5 g per 24 hours, or at least 3+ on dipstick testing, oliguria of lesser than

500 ml per 24 hours, cerebral or visual disturbances, pulmonary edema or cyanosis, epigastric or right upper quadrant pain, impaired liver function, thrombocytopenia, fetal growth restriction(1). Fetal growth restriction is defined as the condition in which the newborn has a birth weight lesser than 10% for gestational age.

Blood collection

Three ml of blood was collected by vein puncture, blood samples were placed into sterile test tubes and left for 30 minutes at 37 °C then were centrifuged at 3000 rpm for 15 minutes then the clot was removed and the obtained sera were then aspirated using automatic micropipette and transferred into clean test tubes and stored in at -20°C for determination of Serum Calcium and Magnesium by Conventional laboratories procedure and manufactures instructions.

RESULTS

As shown in Table 1. There was not a significant difference between the studied cases and the control group in terms of patient age, gestational age at the time of sampling, or parity (P>0.05). On the other hand, there was a significant difference between the studied cases and the control group in terms of systolic and diastolic blood pressure. (P <0.05).

Table 1: Clinical characteristics of studied women

Parameters (Mean±SD)	Pre-eclampsia	Control group
Maternal age (yeas)	31.5±4.34	32.1±4.25
Gestational age(week)	33.6±4.23	34.31±4.15
Parity, median (Range)	2 (1–5)	2 (1–4)
Mean 24 h SBP, mm Hg	147.4±12.76*	108.4±9.15
Mean 24 h DBP, mm Hg	94.23±12.1*	70.36±7.66
Maximal SBP, mm Hg	178.5±23.67*	119.5±8.27
Maximal DBP, mm Hg	117.6±13.5*	75.6±13.3

* Statistically significant differences (p < 0.05) between studies and control group.

SBP, systolic blood pressure; DBP, diastolic blood pressure.

No statistically significant differences existed between groups in (T. Test p = NS).

The study demonstrated that Serum calcium mean was significantly decreased in pregnant women with preeclampsia (8.17 mg/dl) as compared with the control group (9.43 mg/dl) (P. value <0.01), as shown Table 2.

Table 2: Level of the Serum calcium in pregnant women with Preeclampsia and the control group

Serum calcium (mg/dl)	Preeclampsia	Control group
Mean	8.17	9.43
SD.	0.35	0.78
Range	7.3-9.1	7.8-11.8

P. value< 0.01

The study demonstrated that Serum Magnesium mean was significantly reduced in pregnant women with Pre-eclampsia (1.73 mEq/L) as compared with the control group (2.15 mEq/L) (P. value <0.01), as shown Table 3.

Table 3: Level of the Serum Magnesium in pregnant women with Pre-eclampsia and the control group

Serum Mg (mEq/L)	Pre-eclampsia	Control group
Mean	1.73	2.15
SD	0.51	0.69
Range	1.26-3.13	1.51-4.7

P. value< 0.001

Generally, out of 50 preeclmaptic women with the diagnosis of preeclampsia, 33 (66 %) had mild preeclampsia and 17 (34 %) possess severe preeclampsia, Figure 1.

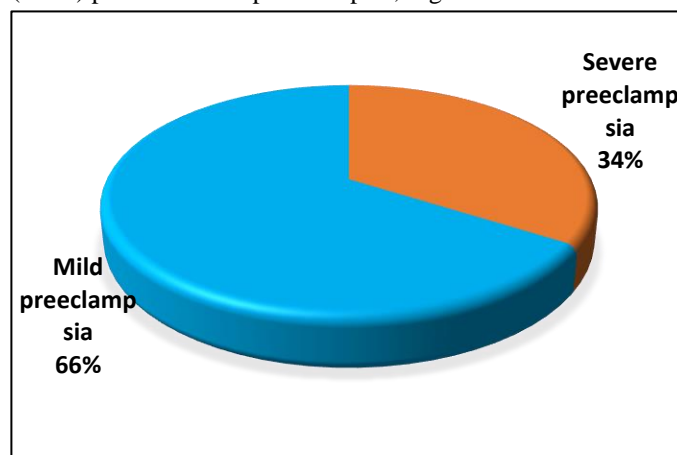


Figure 1: Incidence of severe preeclampsia

The study demonstrated that Serum calcium mean was significantly decreased in pregnant women with severe preeclampsia (8.01 mg/dl) as compared with the mild preeclampsia (9.43 mg/dl) (P. value <0.01), as shown Table 4.

Table 4: Level of the Serum calcium in pregnant women with severe and mild Preeclampsia

Serum calcium (mg/dl)	Mild Preeclampsia	Severe Preeclampsia
No.	33	17
Mean	8.85	8.01
SD.	0.37	0.33

P. value< 0.01

The study demonstrated that Serum Magnesium mean was significantly reduced in pregnant women with severe preeclampsia (1.69 mEq/L) as compared with mild preeclampsia (1.75 mEq/L) (P. value <0.01), as shown Table 5.

Table 5: Level of the Serum Magnesium in pregnant women with severe and mild Preeclampsia

Serum Mg (mEq/L)	Mild Preeclampsia	Severe Preeclampsia
No.	33	17
Mean	1.75	1.69
SD	0.51	0.69

P. value < 0.01

DISCUSSION

The study demonstrated that Serum calcium and magnesium significantly decreased in pregnant women with preeclampsia as compared with the control group (P. value <0.01). The also study demonstrated that Serum calcium and magnesium significantly decreased in pregnant women with severe preeclampsia as compared with the mild preeclampsia. Preeclampsia is one of the most common causes of maternal and fetal morbidities and mortalities ⁽¹⁾. The pathophysiological mechanism is characterized by a failure of the trophoblastic invasion of the spiral arteries, leading to maladaptation of maternal spiral arterioles, which may be associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta ^(4,5). However, the exact etiology of preeclampsia is still unknown. The results from many clinical studies show the relationship between the aggravation of the hypertensive complication and the change in concentration of various chemistries in mother's serum ⁽⁴⁻¹⁰⁾. Interestingly, variable serum calcium and magnesium and are found in preeclamptic mothers ⁽¹¹⁻¹³⁾. 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 the 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. The serum magnesium also decreases in women with preeclampsia ⁽¹⁴⁾. Generally, magnesium has been known as an essential cofactor for many enzyme systems. It also plays an important role in neurochemical transmission and peripheral vasodilatation. Magnesium sulfate appears to be safe and effective for the prevention of seizures and has been used as the drug of choice in severe preeclampsia and eclampsia treatment ⁽¹⁵⁾. Serum calcium level decreases during second and third trimester of pregnancy, primarily due to hemodilution ⁽¹⁶⁾. Some complications of pregnancy may be associated with lower serum calcium level e.g. pre-eclampsia during pregnancy, low birth weight, preterm delivery, and neonatal death ^(17,18). Previous studies have

reported that pre-eclamptic women have lower serum calcium level as compared to normal pregnant women ⁽¹⁹⁾. Study done by Gupta *et al* in North India, however, had concluded that serum calcium level was not associated with pre-eclampsia ⁽¹⁸⁾. The relationship between serum calcium level and pregnancy outcomes is not settled yet. Very few studies in India have reported serum calcium levels among pregnant women ⁽²⁾. Low serum calcium level has been implicated as risk factor for pre-eclampsia in many previous studies ^(19,20). Some other studies have also reported that there is no effect of calcium supplementation on pre-eclampsia ^(7,8). An *et al* did meta-analysis and concluded that there is no effect of calcium supplementation on pre-eclampsia ⁽²¹⁾. The low magnesium levels among preeclampsia women was agreement with study done by Eltayeb *et al* in recent study ⁽²²⁾. Other studies also found similar finding ^(23,24). The data supported the hypothesis that calcium might be a cause in the development of preeclampsia. The effect of serum calcium on changes in blood pressure could be explained by the level of intracellular concentration of calcium. The increase of intracellular calcium concentration when serum calcium went lower led to constriction of smooth muscles in blood vessels and increase of vascular resistance⁽²⁵⁾. The present finding is similar to the previous studies ^(26,27). T present finding was also similar to some studies that the mean serum calcium levels in preeclampsia were not different from normal pregnancy ^(28,29). The difference may be explained by the variations of the studied population and the dietary intake.

CONCLUSIONS

1. The study demonstrated that Serum calcium and magnesium significantly decreased in pregnant women with preeclampsia as compared with the control group.
2. The also study demonstrated that Serum calcium and magnesium significantly decreased in pregnant women with severe preeclampsia as compared with the mild preeclampsia.

RECOMMENDATIONS

1. Nutritional health education should be used as a preventive approach to allow the large sector of the developing countries population to maximize the use of the limited resources in the best way.
2. Advice calcium supplementation during pregnancy specially in those at risk of pre-eclampsia, or those with history of pre-eclampsia

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