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Comparative Cross Sectional Study of Serum Level of Calcium and Magnesium between Preeclamptic and Normotensive Pregnant Women

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ABSTRACT

Background: Preeclampsia (PE), is defined as systemic disease characterized by hypertension, proteinuria and oedema, while 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. Dietary deficiency of Calcium and Magnesium has been shown to play a role in blood pressure regulation and hence establishment of preeclampsia. **Objectives:** The aim of this study was to assess the level of serum Ca+2 and Mg +2 in both normotensive and preeclamptic pregnant women and assess the relationship of these two elements with blood pressure in pregnant women. **Methods:** a comparative cross sectional study was conducted in the department of Obstetrics and Gynaecology /consultation/ at Al-Yarmouk teaching hospital from April to September 2023. This study involved 140 pregnant women of different sociodemographic characteristics, who's gestational age above 20 weeks and registered in local antenatal care clinics. They were interviewed using a questionnaire with different questions. Then every participant was sent to the laboratory. For blood sampling to reveal serum levels of Calcium and Magnesium. **Results:** Serum Ca+2, Mg+2 levels were found to be significantly reduced (<0.01) in the PIH pregnant compared to the normal pregnant women. Also, serum calcium and magnesium levels were significantly reduced in severe preeclamptic women as compared to mild preeclampsia. **Conclusion:** Both serum calcium and magnesium levels in preeclamptic pregnant women were lesser in comparison to healthy pregnant participants. These outcomes support the hypothesis that serum Calcium and Magnesium have been shown to play a role in blood pressure regulation and that hypocalcaemia and hypomagnesaemia are potential etiologic factors incriminated in PIH pathogenesis.

1. Introduction

Preeclampsia (PE), is defined as systemic disease characterized by hypertension, proteinuria and edema, which are thought to be the result of

diffuse endothelial activation and dysfunction ⁽¹⁾. Pregnancy-induced hypertension (PIH) is a new onset of hypertension that appears at 20 weeks or

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more gestational age of pregnancy with or without proteinuria. This major definition includes gestational hypertension, preeclampsia (when it is associated with proteinuria ≥ 30 mg/day or, if not available, a protein concentration ≥ 30 mg ($\geq 1+$ on dipstick) of two random urine samples collected at least 4–6 hours), and eclampsia which is a new onset of generalized tonic-clonic seizures in a woman previously diagnosed with preeclampsia, it can occur antepartum, intrapartum, and postpartum ^(2,3). Globally, PIH represents a significant public health problem contributing to high perinatal deaths, and complicates 2–8% of pregnancies in developed countries, while increasing up to 16.7% in developing countries⁽¹⁾. The previous history of PE, diabetes, multiparity, nulliparity, and maternal age (≥ 40 years) have been shown to increase the risk of PIH. ⁽⁴⁾ Despite the etiology of preeclampsia remains unclear, many reports suggest that abnormal placental implantation and abnormal trophoblastic invasion could be probable causes. ⁽⁵⁾ Dietary deficiency of trace elements has been shown to have negative effects on pregnant mothers and growing fetuses and possibly complicate PE. ⁽⁶⁾

Calcium and Magnesium, as trace elements, are essential micronutrients which should be supplemented on daily basis to all pregnant women. Deficiency or disturbed metabolism of these trace elements can complicate pregnancy and compromise fetal growth. ⁽⁷⁾ Different studies have reported a decreased serum calcium levels in preeclampsia as compared to normal pregnant women. Besides, the association between PIH and serum electrolytes, particularly Calcium (Ca^{+2}) and magnesium (Mg^{+2}) has been reported in many previous studies and there are decreased levels of Calcium and Magnesium in preeclampsia ^(6,8,9). Dietary deficiency of Calcium and Magnesium has been shown to play a role in blood pressure regulation and hence establishment of preeclampsia. ⁽¹⁰⁾ In this study, we aim to provide comparative data on levels of Calcium and Magnesium in pregnant women with PIH and in normal pregnancy.

2. Methods

This is a comparative cross sectional study conducted in the department of Obstetrics and Gynaecology /consultation/ at Al-Yarmouk

teaching hospital from 26th of April to 5th of September 2023. The study involved 140 pregnant women of different sociodemographic characteristics, who's gestational age above 20 weeks and registered in local antenatal care clinics. Inclusion criteria : Pregnant women of gestational age above 20 weeks, carrying their antenatal care cards with them and willing to participate in the study. Exclusion criteria: known diabetic, known hypertensive, history of cardiovascular and/or renal insufficiency, chronic liver disease, infective hepatitis, HIV, TORCH, alcohol consumption, smoker and missed participants.

The sample was conducted conveniently. Each participant was interviewed using a questionnaire with different questions. Weight was taken for each pregnant woman who came for the first visit, using the Camry digital weight scale and prepregnancy weight or first trimester weight were also collected depending on patient memory and their ANC cards information. Height is measured using the tape measure after standing shoeless against the wall. Then, BMI was calculated for each pregnant woman depending on this formula:

Body mass index (BMI) = Weight in k.g / Height ² in cm. ⁽¹¹⁾ Measurement of Blood pressure is done by sphygmomanometer in sitting position, with a cuff size appropriate to patients arm circumference to eliminate a possible stressor for the patients. Pregnancy induced hypertension is defined as systolic blood pressure (SBP) >140 mmHg and diastolic blood pressure (DBP) >90 mmHg. It is classified as mild (SBP 140–149 and DBP 90–99 mmHg), moderate (SBP 150–159 and DBP 100–109 mmHg) and severe (SBP ≥ 160 and DBP ≥ 110 mmHg). ⁽¹²⁾ Finally, Blood samples were taken from each pregnant woman after being examined by the Obs./Gyn. consultant doctor, and sent to the private laboratory near the hospital for serum calcium and magnesium levels.

Statistical analysis

After data collection, all the questions and findings of the study were coded. The data entry was performed using an excel sheet program. Then, the statistical analysis was done using SPSS program version 23. The sample was divided into

two groups ; Pregnant women with PIH and pregnant women without PIH. The data were presented in figures and tables showing the frequency of distribution and percentages of different variables between the two groups of pregnant women. Multivariate regression analysis was used to compare the basic and serum parameters of participants. P values of less than 0.05 were considered statistically significant.

Ethical considerations

First, approval from Arab Board for health specialities was done. Then, A verbal permission was taken from each participant to be included in

the study and answer all the questions and accept to be sent for blood sampling.

3. Results

A total of 140 participants were included in the study. Mean age was 28.62 ± 5.29 years. Out of the total; 115 (82.1%) aged below 35 years, 98 (70.0%) lives in urban

area, 110 (78.6%) Unemployed, 66 (47.1%) Primary education, GA ≥ 32 among 64

(45.7%), 41 (29.3%) Primiparous, 62 (44.3%) Overweight, and 52 (37.1%) obese.

Table 1: Sociodemographic features of participants

Sociodemographic features		No.	%
Age Group/years	<35	115	82.1
	≥ 35	25	17.9
Residency	Rural	42	30.0
	Urban	98	70.0
Occupation	Unemployed	110	78.6
	Employed	30	21.4
Education	Illiterate	23	16.4
	Primary	66	47.1
	Secondary	31	22.1
	Higher education	20	14.3
GA/weeks	20-24	25	17.9
	24-28	25	17.9
	28-32	26	18.6
	≥ 32	64	45.7
Parity	Primigravida	41	29.3
	1	52	37.1
	2	30	21.4
	≥ 3	17	12.1
Had Abortion	Yes	36	25.7
	No	104	74.3
Had Still Birth	Yes	7	5.0
	No	133	95.0
Had CS	Yes	49	35.0
	No	91	65.0
Had Preterm Labour	Yes	20	14.3
	No	120	85.7
BMI category	Normal	26	18.6
	Overweight	62	44.3
	Obese	52	37.1
Total		140	100.0

There were 70 (50.0%) participants without PIH (normotensive) and other 70 (50.0%) participants with PIH [59 (42.1%) with mild PE and 11 (7.9%) with severe PE]. **Figure 1**

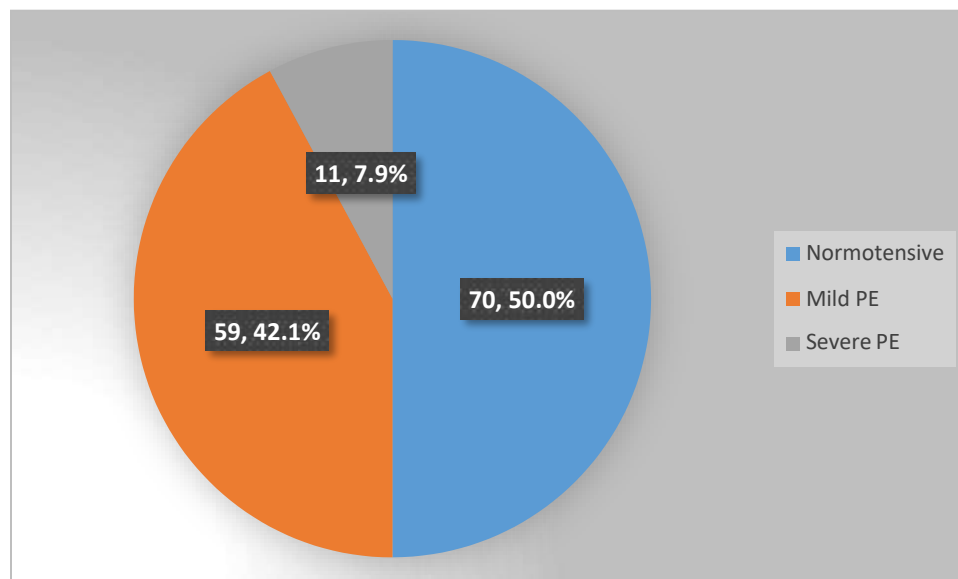


Figure 1: Blood pressure categories among participants

PE was significantly higher among participants aged 35 years and more, with ≥ 3 parties, had Abortion, still birth, CS, and preterm labour; ($P=0.004$, $P=0.001$, $P<0.001$, $P=0.007$, $P=0.021$, and $P<0.001$) respectively.

GA between 20-24 weeks and normal BMI was significantly associated with normal BP (without PE), $P<0.001$.

Table 2: Distribution of sociodemographic features of participants according to the PIH

Sociodemographic features		Pregnant women					P value
		with PIH		without PIH		Total	
		No.= 70	%	No.= 70	%	Count	
	<35	51	44.3	64	55.7	115	0.004
Age Group/years	≥35	19	76.0	6	24.0	25	
Residency	Rural	20	47.6	22	52.4	42	0.71
	Urban	50	51.0	48	49.0	98	
Occupation	Unemployed	52	47.3	58	52.7	110	0.21
	Employed	18	60.0	12	40.0	30	
Education	Illiterate	11	47.8	12	52.2	23	0.54
	Primary	31	47.0	35	53.0	66	
	Secondary	15	48.4	16	51.6	31	
	Higher education	13	65.0	7	35.0	20	
GA/weeks	20-24	5	20.0	20	80.0	25	<0.001
	24-28	8	32.0	17	68.0	25	
	28-32	16	61.5	10	38.5	26	
	≥32	41	64.1	23	35.9	64	
Parity	Primigravida	16	39.0	25	61.0	41	0.001
	1	19	36.5	33	63.5	52	
	2	22	73.3	8	26.7	30	
	≥3	13	76.5	4	23.5	17	
Had Abortion	Yes	30	83.3	6	16.7	36	<0.001
	No	40	38.5	64	61.5	104	
Had still birth	Yes	7	100.0	0	0.0	7	0.007
	No	63	47.4	70	52.6	133	
Had CS	Yes	31	63.3	18	36.7	49	0.021
	No	39	42.9	52	57.1	91	
Had preterm labour	Yes	20	100.0	0	0.0	20	<0.001
	No	50	41.7	70	58.3	120	
BMI category	Normal	3	11.5	23	88.5	26	<0.001
	Overweight	29	46.8	33	53.2	62	
	Obese	38	73.1	14	26.9	52	

PIH was significantly found among older obese participants with mean SBP 151.99±6.03 mmHg and mean DBP 93.37±4.25 mmHg; P<0.001.

Participants without PIH significantly associated with higher levels of Ca and Mg, P<0.001. **Table 3.**

Table 3: Basic and Serum parameters according to PIH.

Variables	Pregnant women		P value
	with PIH	without PIH	
	Mean±SD	Mean±SD	
Age/years	30.60±4.87	26.64±4.97	<0.001
BMI kg/m ²	31.13±4.56	27.23±3.63	<0.001
SBP mmHg	151.99±6.03	109.56±7.31	<0.001
DBP mmHg	93.37±4.25	71.06±5.12	<0.001
Ca (mg/dl)	8.73±0.31	9.84±0.24	<0.001
Mg (mEq/L)	1.33±0.14	1.96±0.20	<0.001

Age, BMI, SBP, and DBP were found to be correlated positively and significantly with each other, and correlated negatively and significantly with Ca and Mg levels; $P < 0.001$. **Table 4.**

Table 4: Multivariate regression analysis according to Basic and Serumparameters of participants

Variables		Age/years	BMI kg/m ²	SBP mmHg	DBP mmHg	Ca	Mg
Age/years	r	1	.540**	.442**	.474**	-.409-**	-.314-**
	P		<0.001	<0.001	<0.001	<0.001	<0.001
BMI kg/m ²	r		1	.466**	.492**	-.507-**	-.378-**
	P			<0.001	<0.001	<0.001	<0.001
SBP mmHg	r			1	.936**	-.916-**	-.883-**
	P				<0.001	<0.001	<0.001
DBP mmHg	r				1	-.875-**	-.827-**
	P					<0.001	<0.001
Ca (mg/dl)	r					1	.885**
	P						<0.001
Mg (mg/dl)	r						1
	P						
**. Correlation is significant at the 0.01 level (2-tailed).							
r=Pearson Correlation							

Mild PE was associated significantly with participants aged less than 35 years, lives in urban area, without preterm labour, and non-obese, (P=0.003, P=0.038, P=0.038, P=0.004) respectively. **Table 5.**

Table 5: Distribution of sociodemographic features of participants according to PE

Sociodemographic features		Pregnant women					P value
		With Mild PE n=59		With Severe PE n=11		Total	
		Count	N %	Count	N %	Count	
Age Group/years	<35	47	92.2	4	7.8	51	0.003
	≥35	12	63.2	7	36.8	19	
Residency	Rural	14	70.0	6	30.0	20	0.038
	Urban	45	90.0	5	10.0	50	
Occupation	Unemployed	43	82.7	9	17.3	52	0.53
	Employed	16	88.9	2	11.1	18	
Education	Illiterate	8	72.7	3	27.3	11	0.71
	Primary	27	87.1	4	12.9	31	
	Secondary	13	86.7	2	13.3	15	
	Higher education	11	84.6	2	15.4	13	
GA/weeks	20-24	5	100.0	0	0.0	5	0.28
	24-28	8	100.0	0	0.0	8	
	28-32	14	87.5	2	12.5	16	
	≥32	32	78.0	9	22.0	41	
Parity	Primigravida	15	93.8	1	6.3	16	0.51
	1	18	94.7	1	5.3	19	
	2	18	81.8	4	18.2	22	
	≥3	8	61.5	5	38.5	13	
Had Abortion	Yes	24	80.0	6	20.0	30	0.39
	No	35	87.5	5	12.5	40	
had still birth	Yes	6	85.7	1	14.3	7	0.91
	No	53	84.1	10	15.9	63	

had cs	Yes	26	83.9	5	16.1	31	0.93
	No	33	84.6	6	15.4	39	
had preterm labour	Yes	14	70.0	6	30.0	20	0.038
	No	45	90.0	5	10.0	50	
BMI category	Normal	3	100.0	0	0.0	3	0.004
	Overweight	29	100.0	0	0.0	29	
	Obese	27	71.1	11	28.9	38	

Severe PE was associated significantly with older participants, had higher mean of BMI, SBP, DBP, Ca, and Mg; $P < 0.05$. **Table 6.**

Table 6: Basic and Serum parameters according to PE.

	BP category		P value
	Mild PE	Severe PE	
	Mean± SD	Mean±SD	
Age/years	29.71±4.63	35.36±3.17	<0.001
BMI kg/m ²	30.44±4.41	34.85±3.53	0.003
SBP mmHg	150.00±4.00	162.64±3.23	<0.001
DBP mmHg	92.17±3.40	99.82±1.83	<0.001
Ca (mg/dl)	8.81±0.26	8.31±0.23	<0.001
Mg (mEq/L)	1.36±0.13	1.21±0.12	0.001

4. Discussion

On the physiological basis, calcium plays a significant role in muscle contraction and regulation of water balance in body tissues. Modification of plasma calcium concentration leads to a change in blood pressure. The lowering of serum calcium and the increase of intracellular calcium can cause an increase in blood pressure in preeclamptic pregnant women. ⁽¹³⁾ This study

demonstrated that Serum calcium significantly decreased in pregnant women with PIH (8.73 ± 0.31) as compared with normal pregnant women, without PIH (9.84 ± 0.24), (P value < 0.01). The study also demonstrated that Serum calcium significantly decreased in pregnant women with severe preeclampsia (8.31 ± 0.23) as compared with the mild preeclampsia (8.81 ± 0.26). These results were corresponded to the results of a study done in Salahaldin, Iraq and two studies

from India.^(14,15,16) A case control study conducted in Egypt 2022 revealed that the mean serum calcium level in the control group was (8.99 ± 0.52) mg/ dl which is higher than the patients group (8.05 ± 0.51) mg /dl, ⁽¹⁷⁾. These results were consistent with our results.

Moreover, Low serum calcium level has been considered as risk factor for preeclampsia in previous studies from Thailand and Canada .^(18,19). In contrast to our results, A Study conducted in Bangladesh in 2013, had concluded that serum calcium level was not associated with preeclampsia.⁽²⁰⁾ Magnesium has been known as an essential cofactor for many enzymes. It also plays an extraordinary role in neurochemical transmission and peripheral vasodilatation. Magnesium Sulphate appears to be effective in the prevention of seizures and safe to be used as a drug of choice in severe preeclampsia and eclampsia treatment.⁽²¹⁾.

In this study, it has been revealed that serum Magnesium level was significantly decreased in pregnant women with PIH (1.33 ± 0.14) as compared with normal pregnant women without PIH (1.96 ± 0.20), (P. value < 0.01). Moreover, serum Magnesium level was significantly decreased in pregnant women with severe preeclampsia (1.21 ± 0.12) as compared with mild preeclampsia (1.36 ± 0.13) . These findings were consistent with the results found in an Iraqi study conducted in Salahaldin in 2022 ⁽¹²⁾ and in Egypt 2022. ⁽¹⁷⁾ Also, The low magnesium levels among preeclamptic pregnant women in this study was similar to studies done in Iran, Sudan and Niger. ^(22, 23, 24). Besides, serum magnesium level in severe preeclamptic women was significantly lower than mild preeclampsia this is consistent with a study done by Chaurasia PP in south India ⁽¹⁶⁾ and Tavana Z in Iran ⁽²²⁾. These differences in serum calcium and magnesium levels among those studies may be explained by the variations in the studied population and the dietary intake of these two elements.

5. Conclusion

Levels of serum Calcium and Magnesium were significantly decreased in women with PIH as compared to normotensive pregnant women. Also, these levels were significantly higher in

pregnant women with mild PE as compared with severe PE women. These outcomes support the hypothesis that serum Calcium and Magnesium levels have been shown to play a role in blood pressure regulation and advice Calcium supplementation during pregnancy especially those at risk of developing preeclampsia or those with history of pregnancy induced hypertension PIH.

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