Al-Azhar Med. J. *Vol. 52(4), October, 2023, 1151-1164*
DOI: 10.21608/amj.2023.326885
https://amj.journals.ekb.eg/article_326885.html

ESTIMATION LEVELS OF SERUM CALCIUM, MAGNESIUM, URIC ACID AND C-REACTIVE PROTEIN IN MILD PREECLAMPSIA COMPARED TO LEVEL NORMAL PREGNANT WOMEN TO EARLY PREDICT SEVER PREECLAMPSIA

By

Mohamed Nour El-Din Mohamed, Ibrahim Abd El-Hamid Abou-Sekein and Attia Mohamed Attia

Department of Obstetrics and Gynecology, Faculty of Medicine, Al-Azhar University

Corresponding author: Mohamed Nour El-Din Mohamed,

E-mail: mohamed_noureldin16@gmail.com

ABSTRACT

Background: Preeclampsia is a common medical disorder affecting about 2–7% of pregnant women worldwide and can lead to unfavorable pregnancy outcomes such as increased maternal as well as perinatal morbidity and morbidity. The etiology of preeclampsia remains ambiguous, albeit, reports that implicated placental defects and oxidative stress early during pregnancy in affected pregnancies. Micronutrients and trace elements play a pivotal role in metabolism and in the preservation of tissue function. Trace elements are important constituents of a number of antioxidants. Therefore, they are integral part of a robust antioxidant that protects the cell from damage.

Objective: To assess association serum levels of calcium, magnesium, uric acid and C-reactive protein in mild preeclampsia ladies and normal pregnant ladies to predict sever preeclampsia.

Patients and methods: This was a case control study was conducted at Al-Azhar university hospitals included 100 patients in their third trimester of gestation divided into two groups; The 1st group consisted of 50 pregnant ladies with preeclampsia in the third trimester of pregnancy that was determined by last menstrual period (LMP) or first trimester ultrasound, and the 2nd group consisted of 50 normotensive pregnant ladies in the third trimester of pregnancy that was determined by last menstrual period (LMP) or first trimester ultrasound. Duration of research was one year starting from May2020 to May 2021.

Results: Calcium and magnesium were significantly lower in preeclampsia group compared to normotensive group. Meanwhile, uric acid and CRP levels were significantly higher in preeclampsia group compared to normotensive group. There a significant positive correlation between DBP with uric acid, CRP and proteinuria while there a significant negative correlation between DBP with calcium and magnesium. Receiver operating characteristic (ROC) curve of UA to predict women with preeclampsia. Best cutoff value for UA is >5.9 mg/dl, which gives a sensitivity of 78% and specificity of 84%. The study revealed that CRP with value > 12 mg/L, has a sensitivity of 85% and specificity of 94%, furthermore, cutoff value for calcium is < 8.9 mg/dl and has a sensitivity of 73% and specificity of 88%, while as regard Magnesium with cutoff value < 1.8 mg/dl has a sensitivity of 70% and specificity of 82%. Calcium, uric acid and CRP were found to be significant predictors for preeclampsia.

Conclusion: Serum C-reactive protein, magnesium and uric acid levels along with blood cell count cumulatively can be measured and may be used as markers for early diagnosis of preeclampsia and can be reduced maternal as well as fetal morbidity and mortality.

Keywords: Preeclampsia, Calcium, Magnesium, Uric acid, C-reactive protein.

INTRODUCTION

Preeclampsia (PE), a complication of late pregnancy, is characterized by hypertension, proteinuria and varying degrees of ischemic end-organ damage. It is one of the leading causes of maternal and fetal morbidity and mortality and currently there is no cure other than termination of the pregnancy. Worldwide about 50,000 mothers die due to pregnancy induced hypertension per year. It is responsible 25%of all fetal growth retardation and 15% preterm birth in developed countries *(Kameswaramma, 2014).*

Preeclampsia (PE) is a disorder, all around characterized by the beginning of hypertension (≥140/≥90 mmHg) and proteinuria (≥0.3 g/24 h) following 20 weeks of development in a formerly normotensive lady that likewise might be related with bunch, different signs and indications, and frequently with subnormal fetal development *(Shamshiraj et al., 2012).*

Preeclampsia has been considered as a disease of unknown pathophysiology. Numerous etiologies have been put forward in light of this serious condition of pregnancy *(Jain et al., 2010).* Altered concentration of various trace elements has been reported during pregnancy (Chaudhari et al, 2018). Serum Ca and Mg are two intracellular ions that are very important for cellular metabolism such as muscles contractibility, secretion, neuronal activity as well as cellular death *(Kesteloot et al., 2011).*

Changes in the levels of Ca, Mg and copper in all the trimesters of pregnancy and zinc during mid and late pregnancy and postpartum period have been reported. Moreover, reduction in serum Ca, Mg and zinc during pregnancy has been attributed as a possible contributor among the various etiologies of PE, therefore supplementation of these elements in diet may be of high value to prevent this devastating condition *(Elmugabil et al., 2016).*

Raised serum uric acid levels because of diminished renal urate discharge are every now and again found in ladies with preeclampsia. Hyperuricemia because of oxidative pressure is known to be related with malicious consequences for endothelial brokenness, oxidative digestion, platelet adhesiveness and conglomeration. Subsequently raised serum uric acid is profoundly prescient of expanded danger of unfriendly maternal and fetal result *(Hawkins et al., 2012).*

C-reactive protein (CRP) is an acute phase protein which is synthesized in hepatocytes and present in trace amount in normal healthy person and rise significantly following injury and inflammation. Endothelial cell dysfunction and inflammation are considered to have a crucial role in the pathophysiology of PE. It has been shown that serum levels of C- reactive protein (CRP) and inflammatory cytokines are elevated in women with PE. CRP in the third trimester is elevated in women with preeclampsia compared to those with normal pregnancies, and levels have been shown to correlate with disease severity *(Cunningham et al., 2010).*

Pre-eclampsia (PE) is a disorder of pregnancy characterized by hypertension with proteinuria after 20 weeks of

pregnancy in previously normotensive and non-proteinuric patients which may progress to seizures (eclampsia) and maternal and foetal death if emergency delivery is not performed. Environmental and nutritional factors may play a role in the aetiology of pre-eclampsia. Pregnant women in the developing countries consume diets with lesser amounts of essential minerals and vitamins. Among all, there exists an alteration in Calcium and magnesium metabolism during pregnancy which could be a potential factor causing pre-eclampsia *(Chaudhari et al., 2018)*.

The aim of this study was to assess association serum levels of calcium, magnesium, uric acid and C-reactive protein in mild preeclampsia ladies and normal pregnant ladies to predect sever preeclampsia.

PATIENTS AND METHODS

The study in al-azhar university hospitals included 100 patients in their third trimester of gestation divided into two groups.

The 1st group consisted of 50 pregnant ladies with preeclampsia in the third trimester of pregnancy that was determined by last menstrual period (LMP) or first trimester ultrasound.

The 2nd group consisted of 50 normotensive pregnant ladies in the third trimester of pregnancy that was determined by last menstrual period (LMP) or first trimester ultrasound. Duration of research is one year starting from May2020 to May 2021

Inclusion criteria: Primigravida age from 18-35 years, gestational age over 28 weeks till 36 weeks, singleton pregnancy, living baby, and patients with serious preeclampsia as indicated by the criteria referenced by the American College of Obstetricians and Gynecologists (ACOG).

Diagnostic criteria of mild preeclampsia are:

- Blood pressure ≥140/90mmHg following 20 weeks development estimated twice 4-6 hours separated in a lady with a formerly typical circulatory strain.
- Proteinuria ≥ 0.3gm/24 hours or ≥ 1+ dipstick pee.

Exclusion criteria:

Pregnant ladies with history of any therapeutic issue, for example, fundamental hypertension, diabetes mellitus, renal infections, cardiovascular sicknesses, endocrine maladies or immune system illnesses, gestational age under 28 weeks or over 40 weeks, multi-fetal pregnancy, intra-uterine fetal demise, history of pre mature ruptured of membranes or clinical chorioamnionitis, pregnant ladies with history of vesicular mole or choriocarcinoma, and patients with Blood pressur ≥ 160/110mmHg. 8.pationt with Proteinuria ≥ 5gm/24 hours or ≥ 3+ dipstick

Ethical consideration:

- The study is approved by the medical ethics committee of Al- Azhar University Hospitals and a written informed consent will be obtained from all participants. After being informed about the aims and process of the study.
- The study procedures are free from any harmful effects on the participants as well as the service provided.

- The principal investigators are kept individual data as private information safely. There were no extra fee to be paid by the participants and the investigators covered all the costs in this regard. An official permission were obtained from Faculty of Medicine, Al- Azhar University.
- An official permission was obtained from the Gynecology and Obstetrics Department.
- An official permission was obtained from the Institutional Research.

Statistical Analysis:

All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows (SPSS Inc, Chicago, IL, USA) & MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean ± SD (Standard deviation) for parametric and median and range for non-parametric data. Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively. Pearson's correlation coefficient was used for correlating normal variables. The (+) sign was considered as indication for direct correlation i.e. increase frequency of independent lead to increase frequency of dependent & (-) sign as indication for inverse correlation i.e. increase frequency of independent lead to decrease frequency of dependent, also we consider values near to 1 as strong correlation & values near 0 as weak correlation. Regression analysis using the stepwise method was used to determine the potential predictors of preeclampsia.

Odds ratio (OR) interpreted with 95% CI is used to determine the association between an exposure and an outcome, representing the odds that an outcome occurred given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure

- OR=1 Exposure does not affect odds of outcome.
- OR>1 Exposure associated with higher odds of outcome.
- OR<1 Exposure associated with lower odds of outcome.

Receiver operating characteristic (ROC) curve was constructed to permit selection of threshold values for test results and comparison of different testing strategies. Areas under ROC curves and their standard errors were determined using the method of Cantor, and compared using the normal distribution, with correction for correlation of observations derived from the same cases. Value of area under a ROC curve (AUC) indicates: 0.90 – 1 = excellent, 0.80-0.90 = good, 0.70-0.80 = fair; 0.60-0.70 = poor; and 0.50-0.6 = fail. The optimal cutoff point was established at point of maximum accuracy. All statistical comparisons were two tailed with significance Level of P-value $\leq$ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates non-significant difference.

RESULTS

There was a significant difference between the groups regarding BMI, SBP, DBP, hemoglobin, PLT, ALT, AST, creatinine and 24h proteinuria.

We found that calcium and magnesium were significantly lower in preeclampsia group compared to normotensive group. Meanwhile, uric acid and CRP levels were significantly higher in preeclampsia group compared to normotensive group **(Table 1)**.

Table (1): Demographic characteristics, clinical data and laboratory parameters among the studied groups

	Preeclampsia (n=50) Mean ± SD	**Normotensive (n=50) Mean ± SD**	**t/χ^2**	**p**
Age (years)	27.33 ± 4.28	25.77 ± 4.54	1.77	0.081
≤ 20 years	12 (24%)	14 (28%)	.486	0.784
21 – 30 years	22 (44%)	23 (46%)		
31 – 35 years	16 (32%)	13 (26%)		
BMI (kg/m^2)	27.12 ± 3.64	26.34 ± 2.39	**2.18**	**0.032**
SBP (mmHg)	147.13 ± 12.44	123.74 ± 11.48	**9.77**	**0.000**
DBP (mmHg)	92.13 ± 8.55	74.39 ± 9.22	**9.98**	**0.000**
Hb (g/dL)	11.19 ± 1.21	11.68 ± 1.17	**2.06**	**0.042**
TLC (x 10^3/L)	8.15 ± 2.32	8.41 ± 2.53	.536	0.594
PLT (x 10^3/L)	287.54 ± 57.76	312.31 ± 45.14	**2.39**	**0.019**
ALT (U/L)	49.22 ± 27.34	26.31 ± 7.76	**5.7**	**0.000**
AST (U/L)	42.37 ± 26.76	23.47 ± 8.33	**4.77**	**0.000**
RBS (mg/dl)	137.75 ± 25.41	139.63 ± 26.88	.359	0.721
Creatinine (mg/dl)	0.82 (0.7 - 1.2)	0.75 (0.6 - 1.1)	**3.75**	**0.001**
Urea (mg/dL)	13.25 ± 3.83	12.47 ± 3.6	1.05	0.297
Proteinuria (mg/dl per 24h)	615.23 ± 142.46	137.57 ± 17.55	**23**	**0.000**
Calcium (mg/dL)	8.42 ± 1.73	9.91 ± 0.847	**5.47**	**0.000**
Magnesium (mg/dL)	1.85 ± 0.386	2.1 ± 0.165	**4.21**	**0.000**
Uric acid (mg/dL)	4.37 ± 2.23	2.87 ± 0.916	**3.99**	**0.000**
CRP (mg/L)	15.23 ± 4.16	5.17 ± 2.55	**14**	**.000**

There was a significant positive correlation between DBP with uric acid, CRP and proteinuria while there a significant negative correlation between DBP with calcium and magnesium **(Table 2)**.

Table (2): Correlation between DBP with other parameters in preeclamptic patients

	DBP	
	r	p
Calcium	**-.300**	**.020**
Magnesium	**-.315**	**.012**
Uric acid	**.521**	**.001**
CRP	**.371**	**.002**
Proteinuria	**.332**	**.005**

There was a significant difference between the groups regarding birth weight only **(Table 3)**.

Table (3): Neonatal outcomes between the studied groups

	Preeclampsia (n=50) Mean ± SD	**Normotensive** (n=50) Mean ± SD	t	**p**
GA (weeks)	37.44 ± 0.927	37.6 ± 0.629	1.01	.315
Birth weight (kg)	2.84 ± 0.435	3.02 ± 0.314	**2.37**	**.019**
Apgar at 1 min	6.73 ± 1.65	7.11 ± 0.964	1.41	.163
Apgar at 5 min	9.71 ± 0.499	9.86 ± 1.21	.811	.419

Receiver operating characteristic (ROC) curve of UA to predict women with preeclampsia. Best cutoff value for UA is >5.9 mg/dl, which gives a sensitivity of 78% and specificity of 84%. The study revealed that CRP with value > 12 mg/L, has a sensitivity of 85% and specificity of 94%, furthermore, cutoff value for calcium is < 8.9 mg/dl and has a sensitivity of 73% and specificity of 88%, while as regard Magnesium with cutoff value < 1.8 mg/dl has a sensitivity of 70% and specificity of 82%. Calcium, uric acid and CRP were found to be significant predictors for preeclampsia **(Table 4)**.

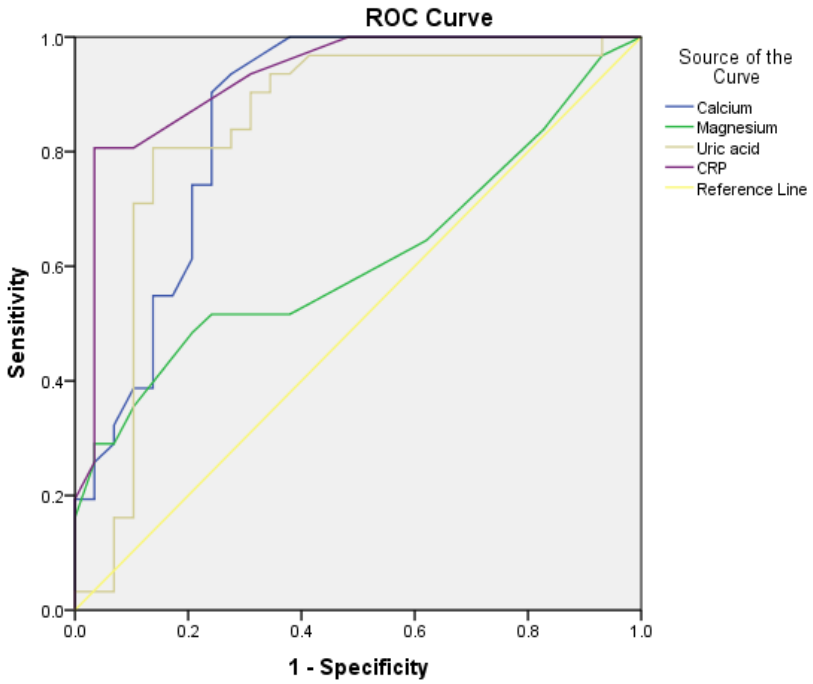

Figure (1): ROC curve of calcium, magnesium, uric acid and CRP as a predictor for preeclampsia

Table (4): ROC curve of calcium, magnesium, uric acid and CRP as a predictor for preeclampsia

Variables	AUC	S.E.	Sig.	95% Confidence Interval	Sensitivity	Specificity
Calcium < 8.9 mg/dl	.859	.051	.000	.759 - .958	73%	88%
Magnesium < 1.8 mg/dl	.615	.074	.126	.471 - .760	70%	82%
Uric acid >5.9 mg/dl	.838	.059	.000	.723 - .953	78%	84%
CRP > 12 mg/L	.928	.034	.000	.861 - .995	85%	94%

Calcium, uric acid and CRP were found to be significant predictors for preeclampsia **(Table 5)**.

Table (5): Multivariate regression analysis to determine the predictors of Preeclampsia

	OR	Sig.	95% CI
Age	1.145	.257	.906 - 1.448
Calcium	.465	**.017***	.039 - 5.592
Magnesium	.573	.436	.046 - 7.167
Uric acid	3.725	**.006***	.117 - 8.321
CRP	.792	**.038***	.636 - .987

DISCUSSION

Analysis of our findings revealed that Mean ± SD of age was 27.33 ± 4.28 in PE group and was 25.77 ± 4.54in normal pregnant women, and mean ± SD of BMI was 27.12 ± 3.64 in PE group, and was 26.34 ± 2.39 in normal pregnant group, there was a significant difference between the groups regarding BMI only.

In agreement with our findings, the study of *Kameswaramma (2014)* aimed to determine the level of C-reactive protein (CRP) in PE mothers along its relation with normal pregnant mothers, and reported that there is no statistically significant difference was observed in mean age, gestational age and BMI between the two groups (p values 0.36, 0.59 and 0.69 respectively.

In another study of *Nair and Savitha (2017)* in which 100 patients out of which 50 were normotensive (control) and 50 had PIH in study group, mean ± SD of age was 22.12± 3.815 years in PE group and was 23.30± 3.460 years in normal pregnant women, there was non-significant difference between the groups regarding age or parity.

In the current study, as expected we found that there was a significant difference between the groups regarding SBP and DBP.

Kameswaramma (2014) study, the mean diastolic blood pressure was also showed significantly higher in women with preeclampsia than in normal pregnant women (p value 0.03). Moreover, *Nair and Savitha (2017)*

confirmed our findings by that systolic and diastolic blood pressure values were higher in the preeclampsia group.

On the other hand, as regard laboratory findings among studied groups, we found that there was a significant difference between the three studied groups regarding hemoglobin, PLT, ALT, AST, creatinine and 24h proteinuria.

In a harmony with our findings, *Mishra et al. (2019)* reported that there was a significant difference between the three studied groups regarding hemoglobin and PLT which were lower in PE group, while ALT, AST, creatinine and 24h proteinuria was higher among PE.

Kameswaramma (2014) reported that there is no significance observed in serum creatinine (p value 0.12) and SGPT (p value 0.06) values in both groups. Positive proteinuria was found in women with PE mothers (1+, 2+), whereas not observed in normal pregnant mothers. The platelet counts were reduced in PE women than normal pregnant mothers, but does not showed difference (p value 0.12). Whereas TLC and neutrophil count was also observed higher in preeclampsia women than normal pregnant women with p value 0.04 & p value 0.04. SGPT also shown significantly higher in preeclampsia compared to control group values (p value0.05).

In the current study, we found that calcium and magnesium were significantly lower in preeclampsia group compared to normotensive group. Meanwhile, uric acid and CRP levels were significantly higher in preeclampsia group compared to normotensive group.

In agreement with our findings, *Kameswaramma (2014)* reported that elevated serum uric acid levels were observed in women with preeclampsia which also correlate with the previous studies of *Cunningham et al. (2010)* and *Kim et al. (2020)*. This may be due to due to decrease renal uric acid excretion. Soluble uric acid impairs nitric oxide generation in endothelial cell, leads to hyperuricemia which can induce endothelial dysfunction (Khosla et al, 2010). Commonly, uric acid is a marker of oxidative stress, tissue injury and renal dysfunction and several studies have reported a positive correlation between elevated maternal serum uric acid levels and adverse pregnancy outcomes *(Thangaratinam et al., 2010)*.

Kameswaramma (2014) study, reduced magnesium levels observed in preeclampsia patient. In the most of the pregnant women, the hypomagnesaemia is associated with hemodilution and renal clearance during pregnancy and consumption of minerals by growing fetus. Magnesium levels may have significant effects on cardiac excitability and on vascular tone, contractility and reactivity *(Kolte et al., 2014)*.

The consequence of low magnesium leads to a reduction in the cerebral blood flow, cerebral vasospasm and neuronal burst increases. Macdonald et al. (2010) shown that magnesium has a vasoprotective effect. These findings support that hypomagnesaemia and hyperuricemia correlate to preeclampsia. There is increasing evidence that preeclampsia is a systemic inflammatory disease.

Punthumapol and Kittichotpanich (2010) reported that the serum calcium in severe preeclamptic women was significantly lower (8.7 +/- 0.59 mg/dl vs. 8.99 +/- 0.31 mg/dl, p = 0.045; and 9.05 +/- 0.52 mg/dl, p = 0 014) and serum uric acid was significantly higher (7.01 +/- 1.93 mg/dl vs. 5.33 +/- 1.23 mg/dl, p < 0.001 and 5.95 +/- 1.9 mg/dl, p = 0.044) than in normal pregnant women and mild preeclamptic women respectively, but there was no difference between normal and mild preeclamptic women. There was no difference in serum magnesium among normal pregnancy and both groups of preeclampsia.

In an examination done by *Khaliq et al. (2018)* there was noteworthy increment in the degrees of serum uric acid in preeclampsia (PE) and they recommended that hyperuricemic levels are autonomously and altogether connected with danger of unfriendly results. Seriousness of preeclampsia increments with expanding uric acid focus.

In the *Abdel-Hamid et al. (2019)* examination, according to preeclampsia seriousness, the mean estimations of CRP were essentially higher in the pregnant ladies with mellow and extreme preeclampsia than in the solid control ladies.

Additionally, the present investigations coincided with that finding revealed by *Sharmin et al. (2016)* who demonstrated that C-reactive protein was 10.28 ± 7.25 mg/mL in mellow PE and 10.94 ± 6.32 mg/mL in extreme PE and 3.45 ± 1.71 mg/mL in normotensive group, which was essentially higher than control group (P = 0.000).

In accordance with previous reports, preeclampsia is associated with increased CRP levels however, there are few studies concerning correlation of CRP levels due to severity of preeclampsia *(Tjoa et al., 2010)*.

Biochemical parameters of *Chaudhari et al., (2018)* study population showed that mean serum total Ca and Mg levels were significantly reduced in pre-eclampsia as compared to the healthy control group. Multi-linear regression analysis of serum Ca, Mg and uric acid showed that serum Ca (regression coefficient= -6.91, p-value=0.001), Mg (regression co-efficient= -16.76, p-value= 0.76) and uric acid (regression coefficient= 4.34, p-value= 0.001) predict the outcome of SBP.

It is worth to be mentioned, in the current study, we found that there a significant positive correlation between DBP with uric acid, CRP and proteinuria while there a significant negative correlation between DBP with calcium and magnesium.

Additionally, this examination in concurrence with study directed by *Begum et al., (2017)* Mean and standard deviation for CRP, systolic and diastolic circulatory strain, were exceptionally huge (p< 0.000 when contrasted and control (5.10±6.20). Also, presumed that CRP demonstrates noteworthy relationship with systolic and diastolic circulatory strain and is a superior indicator of PE and eclampsia.

Furthermore, *Mishra et al. (2019)* reported that Patients with PE without severe features had a positive correlation of hsCRP with DBP, serum bilirubin and serum uric acid level (P values 0.016, 0.034, and 0.029, respectively). In patients

with severe PE however, significantly positive correlation between hsCRP and SBP, DBP, MAP, TLC, SGOT, SGPT, serum bilirubin, blood urea, serum creatinine, serum uric acid, and S/D ratio was noted. A negative correlation between hsCRP and baby weight was found, also there were positive and negative correlation of hsCRP with the DBP and baby weight.

In addition to above findings, in the current study we demonstrated that there was a significant difference between the groups regarding birth weight only.

This comes in comparison with the study of *Abdel-Hamid et al. (2019)* which reported that the mean neonatal birth weight was essentially lower in the pregnant ladies with preeclampsia than in the sound control ladies (2.8 versus 3.01, separately, p0.05). As to score, the mean Apgar score at 1 moment was fundamentally lower in the patients with preeclampsia than in the solid control ladies (8.5 versus 8.9, individually, p0.05), while, there was no critical contrast between the two gatherings in regards to Apgar score at 5 minutes (p>0.05).

In the current study, Receiver operating characteristic (ROC) curve of UA to predict women with preeclampsia. Best cutoff value for UA is >5.9 mg/dl, which gives a sensitivity of 78% and specificity of 84%. The study revealed that CRP with value > 12 mg/L, has a sensitivity of 85% and specificity of 94%, furthermore, cutoff value for calcium is < 8.9 mg/dl and has a sensitivity of 73% and specificity of 88%, while as regard Magnesium with cutoff value < 1.8 mg/dl has a sensitivity of 70% and specificity of 82%.

In a study of *Khosrowbeygi et al. (2011)* reported that ROC curve of UA to predict women with preeclampsia. Best cutoff value for UA is 5.5 mg dL-1, which gives a sensitivity of 65.2% and specificity of 71.1%. UA with a cutoff point of 5.5 mg dL-1 identified women with preeclampsia with sensitivity of 65.2% (95% CI, 42.8-82.8) and specificity of 71.1% (95% CI, 55.5-83.2). Its negative predictive value of 80% (95% CI, 63.9-90.4) was high; the positive predictive value of 53.6% (95% CI, 34.2-72) was low. The study revealed that when UA and CRP were high the risk of preeclampsia was high. The adjusted odds ratio was 4.62 (95% CI, 1.58-13.5; p> 0. 001) and 13.33 (95% CI, 3.41-52.09; p>0.001), respectively and 4.59±0.91 mg dL-1 (severity 3+). These values were smaller than the maximal level reported in our study (6.01 mg dL-1).

Finally, in our study we demonstrated that calcium, uric acid and CRP were found to be significant predictors for preeclampsia.

Elmugabil et al. (2016) reported that a low calcium (OR = 0.73, 95% CI = 0.56 ─ 0.95, P = 0.021) and a high magnesium (OR = 5.724, 95% CI = 1.23 ─ 26.50, P = 0.026) levels were associated with preeclampsia.

Chaudhari et al. (2018) revealed that multinomial regression analysis of the study variables in Pre-eclampsia depicts that the level of serum Ca, Mg and uric acid is not associated significantly with the severity of pre-eclampsia i.e. from mild to moderate or mild to severe pre-eclampsia, their findings suggested that

decrease in serum Ca level is associated with increase in severity of pre-eclampsia, though the association was statistically insignificant.

The study of *Abdel-Hamid et al. (2019)* demonstrated that the mean estimations of serum CRP and serum uric acid were essentially higher in the pregnant ladies with preeclampsia than in the sound control ladies, The mean serum magnesium didn't demonstrate huge contrasts between pregnant ladies with preeclampsia and sound control ladies, these discoveries bolster the theory that hypocalcaemia, hyperuricemia and expanded C-reactive protein are potential causes and results of preeclampsia. Likewise, these discoveries bolster that expanded serum uric acid and serum CRP and diminished serum calcium connect to seriousness of preeclampsia.

CONCLUSION

The present study reveals that there is evidence of inflammation in preeclampsia. High CRP level calcium and uric acid were found to be significant predictors for preeclampsia associated with severe preeclampsia; they correlated positively and significantly with the severity of disease in preeclampsia. Serum C-reactive protein, magnesium and uric acid levels along with blood cell count cumulatively can be measured and may be used as markers for early diagnosis of PE and can be reduced maternal as well as fetal morbidity and mortality.

REFERENCES

1. **Abdel-Hamid MA, Abd El Moneim MZ, Fahd AA and Mekky AM. (2019):** Serum Calcium, Magnesium, Uric Acid and C-Reactive Protein in Preeclampsia and Normal Pregnant Women. The Egyptian Journal of Hospital Medicine, 77 (1): 4847-4854.
2. **Begum G, Zaman N and Khan R. (2017):** Correlation of C-reactive protein with severity of preeclampsia. KJMS, 10(3): 337-41.
3. **Chaudhari R, Apeksha N, Mahima B, Jouslin B and Madhab L. (2018):** Serum Calcium and Magnesium levels in Pre-eclampsia. National Journal of Laboratory Medicine, 7: 1-6.
4. **Cunningham F, Leveno K, Bloom SL, Hauth J, Rouse D and Spong C. (2010):** Pregnancy hypertension. Williams Obstetrics, 23:706-755.
5. **Elmugabil A, Hamdan HZ, Elsheikh AE, Rayis DA, Adam I and Gasim GI. (2016):** Serum Calcium, Magnesium, Zinc and Copper Levels in Sudanese Women with Preeclampsia. PloS One, 11(12): 167-173.
6. **Hawkins TL A, Roberts JM and Mangos GJ. (2012):** Plasma Uric Acid remains a marker of poor outcome in hypertensive pregnancy: A Retrospective cohort study. BJOG, 119:484-492.
7. **Jain S, Sharma P, Kulshreshtha S, Mohan G and Singh S. (2010):** The role of calcium, magnesium, and zinc in preeclampsia. Biol Trace Elem Res, 133:162-70.
8. **Kameswaramma K. (2014):** Estimation of C - Reactive Protein, Magnesium and Uric Acid Levels in PreEclampsia Patients in Comparison with Normal Pregnant Women. Scholars J Applied Med Sci, 2(2): 628-32.
9. **Kesteloot H, Tzoulaki I, Brown IJ, Chan Q, Wijeyesekera A and Ueshima H. (2011):** Relation of urinary calcium and magnesium excretion to blood pressure: the international study of macroand micro-nutrients and blood pressure and the international cooperative study on salt, other factors, and blood pressure. Am J Epidemiol, 174(1):44-51.
10. **Khaliq O, Konoshita P and Moodley J. (2018):** The role of uric acid in preeclampsia: Is uric acid a causative factor or a sign of preeclampsia? Current Hypertension Reports, 20(9): 80-84.

11. **Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C and Mu W. (2010):** Hyperuricemia induces endothelial dysfunction. Kidney International, 67: 1739-1742.

12. **Khosrowbeygi A, Lorzadeh N, Ahmadvand H and Shiravand Y. (2011):** Homocysteine and its association with lipid peroxidation and leptin in preeclampsia. Int J Biol Chem, 5: 184-192.

13. **Kim YB, Jung WW, Lee SW, Jin X, Kang HK, Hong EH and Kim YI. (2020):** Excessive maternal salt intake gives rise to vasopressin-dependent salt sensitivity of blood pressure in male offspring. Journal of Molecular and Cellular Cardiology, 150: 12-22.

14. **Kolte D, Vijayaraghavan K, Khera S, Sica D, Frishman W. (2014):** Role of Magnesium in Cardiovascular Diseases. Cardiology in Review, 22. 182-192.

15. **Macdonald RL, Curry DJ, Aihara Y, Zhang Z-D, Jahromi BS and Yassari R. (2010):** Magnesium and experimental vasospasm. Journal of Neurosurgery, 100:106-110.

16. **Mishra N, Pradhan K, Sahoo GD, Rohilla M and Meena M. (2019):** Can hsCRP be the sole investigation for predicting the severity and outcome in women with pre-eclampsia presenting late in pregnancy? Trop J Obstet Gynaecol., 36:54-60.

17. **Nair A and Savitha C. (2017):** Estimation of Serum Uric Acid as an Indicator of Severity of Preeclampsia and Perinatal Outcome. J Obstet Gynecol India, 67: 109–118.

18. **Punthumapol C and Kittichotpanich B. (2010):** Serum calcium, magnesium and uric acid in preeclampsia and normal pregnancy. J Med Assoc Thai., 91(7):968-73.

19. **Shamshiraj AA, Paidas M and Krikun G. (2012):** Preeclampsia, hypoxia, thrombosis and inflammation. J Pregnancy, 12:374-78.

20. **Sharmin S, Chy S, Alam D, Rashid F, Kabir S. (2016):** Association of Serum C-reactive Protein in Preeclampsia and its Effect on Fetal Birth Weight A Case Control Study. Bangladesh Journal of Obstetrics & Gynaecology, 31(2): 75-80.

21. **Thangaratinam S, Ismail K, Sharp S, Coomarasamy A and Khan K. (2010):** Accuracy of serum uric acid in predicting complications of pre-eclampsia: a systematic review. BJOG: An International Journal of Obstetrics & Gynaecology, 113: 369-378.

22. **Tjoa ML, Van Vugt JMG, GO ATJ, Blankenstein MA, Oudejans CB and Van Wijk IJ. (2010):** Elevated C-reactive protein levels during first trimester of pregnancy are indicative of preeclampsia and intrauterine growth restriction. J Reprod Immunol., 59: 29-3.

تقييم مستوي الكالسيوم والماغنسيوم وحمض اليوريك والبروتين التفاعلي في حالات تسمم الحمل البسيطه مقارنة في طبيعة الحمل من اجل الكشف المبكر لحالات تسمم الحمل المتقدمه

محمد نور الدين محمد، ابراهيم عبد الحميد أبو سكين، عطيه محمد عطيه

قسم أمراض النساء والتوليد، كلية الطب، جامعة الازهر

E-mail: mohamed_noureldin16@gmail.com

خلفيـــة البحـــث: تســمم الحمــل هــو اضــطراب طبــي شــائع يصــيب حــوالي 2-7٪ مــن النســاء الحوامــل فــي جميــع أنحــاء العــالم ويمكــن أن يــؤدي إلــى نتــائج غيــر مواتيــة للحمــل مثــل زيــادة المراضــة والمراضــة الأموميــة وحــديثي الــولادة. تظــل مســببات تســمم الحمــل غامضــة، وإن كانــت تشــير إلــى وجــود عيــوب فــي المشــيمة والإجهــاد التأكســدي فــي وقــت مبكــر أثنــاء الحمــل فــي حــالات الحمــل المصــابة. تلعــب المغــذيات الدقيقــة والعناصــر النــزرة دورًا محوريًــا فــي عمليــة التمثيــل الغــذائي وفــي الحفــاظ علــى وظيفــة الأنســجة. العناصــر النــزرة هــي مكونــات مهمــة لعــدد مــن مضــادات الأكســدة. لــذلك فهــي جزء لا يتجزأ من مضادات الأكسدة القوية التي تحمي الخلية من التلف.

الهــدف مــن البحــث: تقيــيم مســتويات مصــل الــدم المرتبطــة بالكالســيوم والمغنيســيوم وحمــض البوليــك والبــروتين التفــاعلي ســي فــي الســيدات المعتدلــة مــن تســمم الحمــل والسيدات الحوامل العاديات للتنبؤ بتسمم الحمل الحاد.

المريضــات وطــرق البحــث: هــذه دراســة حالــة تــم إجراؤهــا فــي مستشــفيات جامعــة الأزهــر وتضــمنت 100 مــريض فــي الثلــث الثالــث مــن الحمــل مقســمة إلــى مجمــوعتين. تألفــت المجموعــة الأولــى مــن 50 ســيدة حامــل مصــابات بمقــدمات الارتعــاج فــي الثلــث الثالــث مــن الحمــل والتــي تــم تحديــدها مــن خــلال آخــر دورة شــهرية أو الموجــات فــوق الصــوتية فــي الثلــث الأول مــن الحمــل ، والمجموعــة الثانيــة تتكــون مــن 50 ســيدة حامــل معتدلــة الضــغط فــي الثلــث الثالــث مــن الحمــل التــي تــم تحديــدها. بحلــول آخــر دورة شــهرية أو الموجــات فــوق الصــوتية فــي الأثلــوث الأول. كانــت مــدة البحــث ســنة واحــدة تبدأ من مايو 2020 إلى مايو 2021.

نتـــائج البحـــث: كـــان الكالســـيوم والمغنيســـيوم أقـــل بكثيـــر فـــي مجموعـــة تســـمم الحمـــل مقارنـــة بالمجموعـــة المعتدلـــة. وفـــي الوقـــت نفســـه، كانـــت مســـتويات حمـــض البوليـــك و البـــروتين التفـــاعلي ســـي أعلـــى بشـــكل ملحـــوظ فـــي مجموعـــة مقـــدمات الارتعـــاج مقارنـــة بالمجموعـــة العاديـــة. هنـــاك علاقـــة ارتبـــاط موجبـــة معنويـــة بـــين الضـــغط الانبســـاطي مـــع حمـــض البوليـــك، البـــروتين التفـــاعلي ســـي والبـــروتين بينمـــا هنـــاك علاقـــة ســـلبية معنويـــة بـــين الضـــغط الانبســـاطي مـــع الكالســـيوم والمغنيســـيوم. منحنـــى الـــروك لحمـــض اليوريـــك للتنبـــؤ بالنســـاء المصـــابات بمقـــدمات الارتعـــاج. أفضـــل قيمـــة حديـــة لـــ لحمـــض اليوريـــك هـــي> 5.9 مجـــم / ديســـيلتر ، ممـــا يعطـــي حساســـية بنســـبة 78٪ ونوعيـــة 84٪. أوضـــحت الدراســـة أن البـــروتين التفـــاعلي ســـي بقيمـــة> 12 مجـــم / لتـــر، لـــه حساســـية 85٪ ونوعيـــة 94٪، عـــلاوة علـــى ذلـــك ، فـــإن قيمـــة القطـــع للكالســـيوم <8.9 مجـــم / ديســـيلتر ولديـــه حساســـية 73٪ ونوعيـــة 88٪. فـــي حـــين أن المغنيســـيوم ذو قيمـــة القطـــع <1.8 ملـــغ / ديســـيلتر لديـــه حساســـية 70٪ وخصوصـــية 82٪. تـــم العثـــور علـــى الكالســـيوم وحمـــض البوليـــك و البـــروتين التفـــاعلي ســـي لتكـــون مؤشـــرات مهمـــة لتســـمم الحمل.

الاســـتنتاج: يمكـــن قيـــاس مســـتويات البـــروتين التفـــاعلي ســـي فـــي الـــدم والمغنيســـيوم وحمـــض البوليـــك جنبًـــا إلـــى جنـــب مـــع عـــدد خلايـــا الـــدم بشـــكل تراكمـــي ويمكـــن اســـتخدامها كعلامـــات للتشـــخيص المبكـــر لمقـــدمات الارتعـــاج ويمكـــن تقليـــل معـــدلات الاعتلال والوفيات لدى الأمهات والجنين.

الكلمـــات الدالـــة: تســـمم الحمـــل، الكالســـيوم، المغنيســـيوم، حمـــض البوليـــك، بـــروتين ســـي التفاعلي.