International Journal of Academic Multidisciplinary Research (IJAMR)
ISSN: 2643-9670
Vol. 7 Issue 5, May - 2023, Pages: 85-90

Uric acid level and Blood urea Nitrogen/Creatinine Ratio in Pre-eclamptic Ladies (Sudan)

Maazza Omer Adam [1], Rehab Omer A. M. Gibla[2]

[1] Sudan University of Science and Technology, College of Medical Laboratory Science
[2] University of El-Imam El-Mahdi, Department of Haematology and Immune, College of Medical Laboratory Science

Abstract: *Pre-eclampsia is a pregnancy related syndrome; and one of the hypertensive disorders associated with different organ involvement, marked by new onset hypertension and protein-urea. This work was conducted as a cross sectional comparative study aiming to assess, uric acid level and blood urea nitrogen/creatinine ratio in pre-eclamptic women visiting Om-dorman maternity hospital from March to June 2022 . The samples were collected from (130) pregnant ladies, eighty (80) of them were diagnosed as pre-eclampsia cases and (50) were non-pre-eclamptic (control). Uric acid levels, urea and creatinine were measured. Blood urea nitrogen and urea nitrogen/creatinine ratio were calculated. The obtained results were statistically analyzed using (SPSS) program. Significant increase in uric acid level was shown among the pre-eclamptic (7.11±2.08 mg/dl) compared to the control group (3.65 ± 1.06 mg/dl) with p. value (0.000). On the other hand Blood urea nitrogen creatinine ratio showed insignificant increase in the pre-eclampsia group (14.92 ± 5.56), compared to that of control (12.91 ± 7.32) with p. value as (0.099). The levels of urea, creatinine and blood urea nitrogen were significantly increased in the pre-eclamptic cases than the control, with p. values (0.001, 0,022 and 0.001) respectively. No correlation was shown between age and pre-eclampsia phenomena.*

Keywords: Pre-eclampsia, Nitrogen /Creatinine Ratio,Uric acid , Urea nitrogen, Correlation

Introduction

Pre-eclampsia is a pregnancy multifactorial syndrome marked by the advent of new-onset hypertension and protein urea after the 20th week of gestation. It may be accompanied by edema and hyperuricemia, or high blood pressure (Beheiry H.M. *et al*., 2018, Hamed S. *et al*., 2022*).* The most characteristic symptoms are headache or fever with or without visual disturbance. Severe pre-eclampsia also associated with epigastric pain (Beheiry HM *et al*., 2018, Osman *et al*., 2021). Pre-eclampsia damages the liver, kidney and blood coagulation system (Bohan Lv *et al*., 2022). It is a high blood pressure disorders during pregnancy, which are the most potential complications in preterm delivery, perinatal mortality, maternal mortality, intra-uterine growth retardation, low birth weight and many other related problems and it may continue undetected until developing into, convulsion, coma or both due to microvascler involvement **(**Hidajet pacarizi *et al*., 2012, Dr**.** Archana Dhok *et al*., 2019, Moghaddas *et al*., 2019). Pre-eclampsia was reported as one of the top five causes of maternal and perinatal mortality worldwide where it claims the lives of more than 70,000 women and more than 500,000 of their fetuses and newborns per year, which is equivalent to the loss of 1600 lives per day. More than 99% of these losses occur in low- and middle-income countries (LMICs), especially those on the Indian subcontinent and Sub-Saharan Africa, where it was estimated that for every woman who dies, there are another 20women suffer a life-altering morbidity (L. A. Magee *et al.*, 2016).

Hypertensive pregnancy complications make a great risk of developing cardiovascular disease (CVD), metabolic diseases, stroke, and end-stage renal disease (ESRD) later in life. The risk of developing ESRD in women with pre-eclampsia is at 5-12-fold (Mark W *et al.*, 2018). Pre-eclampsia is the most potential complication in preterm delivery, perinatal mortality, maternal mortality, intra-uterine growth retardation, low birth weight and many other related problems, that can dramatically develop into eclampsia, which is more complicated and life threatening to mothers and fetuses. There are few published data regarding preeclampsia prevalence and effect in renal structure and function in Sudan. This study was aimed to give more knowledge about functional kidney changes among pre-eclamptic women in Sudan. Normal pregnancy is associated with physiological and hormonal changes that affect nearly every organ system and it may lead to many biochemical changes (Mohammed *et al.*, 2022). It was widely accepted that placental development is disrupted in some pregnancies affected by pre-eclampsia, leading to cellular, molecular, immunological, and vascular changes. Early-onset pre-eclampsia is classically thought to be mediated by abnormal placentation and shallow trophoblastic invasion within the uterus, thereby resulting in incomplete spiral artery remodeling (Opichka, M.A 2021). Hypertension is one of the common complications that met within normal pregnancy, maternal arterials blood pressure decreases during first trimester and reaches it is lowest point during the second trimester, then increases to pregnancy level during last two months (Nan H. Triano *et al.*, 2018). Hypertension is clinically defined as a change in blood pressure recorded at two different occasions; systolic blood pressure at 140 mmHg or more, diastolic blood pressure at 90mmHg or more, Hypertensive disorders during pregnancy include chronic hypertension, gestational hypertension, pre-eclampsia and chronic hypertension with superimposed pre-eclampsia. The classification of hypertension disorders mainly depends on the time of the onset of the disorder, whether it occurs before or after 20 weeks of gestation (Osman *et al.*, 2021, J.A. Hutcheon *et al.*, 2011). Hypertension disorders significantly contribute to the causes of maternal, perinatal, morbidity and mortality. The gestational hypertension is a common first clinical presentation of pre-eclampsia (Harsida Gosai *et al.*, 2021). Pre-eclampsia as systemic syndrome of pregnancy was suggested to be a disease of placenta (A. Oloruntoba *et al.*, 2018). The exact origin of pre-eclampsia is a point of debate. Maternal disorders such as, hypertension, renal

disease, overweight, and diabetes are only predisposing factors (L. A. Magee *et al.,* 2016). According to H. Moghaddas *et al.,* (2019) Pre-eclampsia is specified by systemic maternal endothelial dysfunction, thrombotic microangiopathy and organ involvement with different clinical syndromes, such as eclampsia, hemolysis, elevated liver function, low platelet counts (HELLP syndrome), and endothelial swelling (kidney, glomerular involvement). Poor trophoblastic invasion and deficient spiral artery remodeling lead to placental ischemia-reperfusion injury and the release of various angiogenic, oxidative, and inflammatory mediators into maternal circulation, promoting generalized endothelial dysfunction, increased vascular reactivity, and activation of the coagulation cascade (Bellos *et al.,* 2020) . One cause of pre-eclampsia can be considered the dis- balance between prostacyclin (prostaglandin I2) and thromboxane A2, as active metabolites of arachidonic acid. This dis-balance causes vasospasms as a central change in pre-eclampsia (Hidajet Paçarizi *et al.,* 2012). Inability of the trophoblastic cells to invade spiral arteries properly causes loss of vessel surface area and the ability to remodel and expand resulting in a decrease in utero placental blood flow. The decreased blood flow deprives the fetus from essential nutrients and oxygen necessary for growth and development. Oxygen deficiency results in placental ischemia, which cause releasing of several factors such as inflammatory cytokines, (TNF, angiotensin II), reactive oxygen species and T helper 1 , T helper 17 cells, in addition to antiangiogenic factors as soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin, which lead to endothelial dysfunction and subsequently pre-eclampsia (Mark W. Cunningham *et al*., 2022). Women suffering pre-eclampsia during their first pregnancy had 4.7 risk ratio of developing end stage renal disease (ESRD) in their later life (Vikse et al., 2008). Nulliparity, Placental and Preexisting maternal are Pregnancy-specific factors. Risk factors include age, high body mass index, Pre-gestational diabetes (type 1 and type 2) which, associated with two to four fold increased risk of pre-eclampsia, Chronic hypertension, Renal disease, antiphospholipid antibody syndrome, connective tissue disorder, family or personal history of pre-eclampsia. Placental factors such as excess placental volume, and multifetal gestation, are also associated with the development of pre-eclampsia where the risk may increase progressively with each additional fetus**.** The risk for pre-eclampsia was suggested to be double if the woman has a partner aged >45 years (Arun Jeyabalan., 2013, UV Ukah, *et al.,* 2016).

Methodology

The study population included (130) pregnant women, (80) of them were confirmed as pre-eclampsia patients and (50) were normotensive. The two groups were ranging from 13-45 years in age and had more than 20 weeks of gestation .Under aseptic conditions, 3ml of venous blood were collected in lithium heparin containers, centrifuged at 3000rpm for 10 minutes, and the clear plasma was analyzed for blood urea, creatinine and uric acid, using Mindray 380.The results were statistically analyzed.

Results and discussion

As shown by figure (1) the frequency distribution of the ages ranging from (21- 28years) represents the highest percentage (43.8%), followed by those ranging from (29- 36years) as (36.20%), (13- 20 years) as (13.8%) whereas that with age range (37- 45years) was the lowest (6.2%).

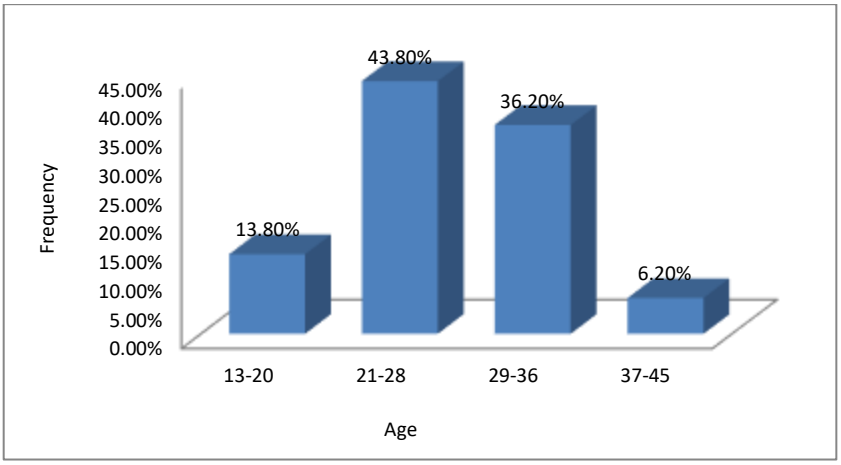

Fig. 1 Frequency distribution of age grouping

Table (1) shows the means of the different parameters for the first pregnancy cases as, age (23.12years), systolic blood pressure (152.51), diastolic blood pressure (98.83), urea (25.02), creatinine (0.84), uric acid (6.77), BUN (11.37), BCR (14.40). The systolic and diastolic blood pressure was higher than the normal ranges.

Table 1. Mean values of variables for first pregnancy cases

Variables of Primagriva	Means± STD	Normal range
Age (years)	23.12 ±5.53	_
Systolic Blood pressure	152.51 ± 28.17	<120mmHg
Diastolic Blood pressure	98.83 ± 17.74	<90mmHg

Urea	25.02 ± 14.79	20-50 mg/dl
Creatinine	0.84 ± 0.57	0.4-1.4 mg/dl
Uric acid	6.77 ± 2.31	3.5-7.2 mg/dl
BUN	11.37 ± 6.58	7-20 mg/dl
BCR	14.40 ± 5.48	10:1 -20:1

For the total study population the gestation number which ranges from (1-3) represents the higher percentage (69.2%) followed by those ranging from (4-6) as (24.6%) whereas those ranging from (7-10) were the lowest (6.2%) as shown by (table 2).

Table 2. Gestation numbers for total population (%)

Gestation No.	Percentage
1-3	69.2%
4-6	24.6%
7-10	6.2%
Total	100.0

Table (3) shows that, the women having one child death represent (21.5%), two child death (6.2%) ,three child death (2.3%), four child death (0.8%) and five child death (2.3%), whereas those with no child death history represents (66.9%).

Table 3. Previous child death for the total study population

Death	Frequency	Percentage
No death	87	66.9%
1	28	21.5%
2	8	6.2%
3	3	2.3%
4	1	0.8%
5	3	2.3%
Total	130	100.0

Table (4) shows, the frequency distribution of hypertensive cases where, those with hypertension history were (18.7%).

Table 4. The cases with hypertension history

Hypertension	Frequency	Percentage
No	65	81.3%
Yes	15	18.7%
Total	80	100%

Among the study population the delivery by Caesarean section represents (62.3%) while the normal delivery was (37.7%) as shown by table (5).

Table 5. Delivery type among the study population

Delivery	Frequency	Percentage
Normal	49	37.7%
Caesarean	81	62.3%
Total	130	100.0

Table (6). Shows that, the mean values of the measured parameters were higher in the cases with hypertension history than the normal ranges. This may indicate the effect of hypertension before or/and after pregnancy period on the different parameters.

Table (6). The effect of hypertension history on the different Parameters

Parameter	History HTN Mean	New HTN Mean	Normal range
SBp(mm Hg)	180.66	159.66	<120mmHg
DBp(mm Hg)	108.66	101.03	<90mmHg
Urea(mg/dl)	22.60	29.13	20-50 mg/dl
Creatinine(mg/dl)	0.78	1.08	0.4-1.4 mg/dl
Uric acid(mg/dl)	6.3200	7.29	3.5-7.2 mg/dl
Blood urea Nitrogen(mg/dl)	10.49	13.34	7-20 mg/dl
BUN/Creatinine Ratio	15.16	14.87	10:1 -20:1

Plasma uric acid

As shown by table (No.7) the uric acid is significantly increased in the preeclampsia group than the control with p.value (0.000) at 5% level of significant. Hamed et al., (2022), reported significant increasing of serum uric acid in pre-eclamptic cases. The study of Mostafa, et al., (2019), showed high Serum uric acid (p<0.0) in pre-eclamptic. The results obtained in this study were strongly agree with, Sujata Sahav, *et al*., (2018), Al-Jameil N, (2014), Deepika Kapil *et al*., (2021), Amir Shakarami *et al*., (2020), Wadhwani R *et al*., (2021), Hidajet Paçarizi *et al*., (2012), Akram Elkhair et al, (2016) and Oloruntoba Ayodele Ekun *et al*., (2018).

Table 7. The differences in parameter means between the preeclamptic and control in the study population.

Parameter	t-test	Control (Mean±SD)	Case (Mean±SD)	p. value
Urea(mg/dl)	2.895	17.50 ± 6.25	27.91±24.91	0.001
Creatinine(mg/dl)	1.868	0.68±0.6880	1.03 ± 1.28	0.022
Uric acid(mg/dl)	10.878	3.65 ± 1.06	7.11 ± 2.08	0.000
BUN(mg/dl)	2.790	8.14 ± 2.91	12.88±11.77	0.001
BCR	1.773	12.91 ± 7.32	14.92 ± 5.56	0.099

Blood urea nitrogen creatinine ratio

Table (7) showed insignificant increase in Blood urea nitrogen/creatinine ratio (BCR) in the preeclamptic cases with p. value (0.099 > 0.05) at 5% significance level, this may disagree with Hidajet Paçarizi et al., (2012) and Al-Jameil N (2014) who reported significant increase of BCR. According to Neil Baum (1975), the preservation of the blood urea nitrogen/serum creatinine ratio of (10:1) during pregnancy, may be attributed to the increase of GFR and decrease of tubular re-absorption of urea, which is a result of an expanded circulating blood volume present in the pregnant woman.

Urea

Urea shows significant difference between the cases and control group (p=0.001) (table.7). The increase of serum urea level in pre-eclamptic was reported by, Hidajet Paçarizi et al.,(2012), Julie Sarmah (2018) and Oloruntoba A. et al., (2018).

Creatinine

The mean of creatinine levels showed significant increase in the pre-eclamptic cases compared with the control (P=0.022), which was less than (0.05). Julie Sarmah (2018), Al Jameil N., (2014) and Oloruntoba Ayodele Ekun et al., (2018) reported significant increase with (p<0.05), in the mean of creatinine among pre-eclamptic patients when compared with normotensive control, this may disagree with, Hidajet Paçarizi et al., (2012), Ranjit S., Archana (2019). Pearson correlation values show that, there is no significance correlation between age, uric acid level and BCR, Table (8).

Table 8. Correlation of age with uric acid and BCR

Age	Uric acid	BCR
Pearson Correlation	-0.144	0.005
p-value	0.10	0.95

As shown by Table (9), the significant correlation of the systolic blood pressure with urea (P= 0.037) blood urea nitrogen (P=0.043), and uric acid (P=0.000). On the other hand, insignificant correlation between the systolic blood pressure and creatinine (P=0.271).

Table 9. Pearson correlation between systolic blood pressure and urea, creatinine, uric acid, BUN and BCR in the preeclamptic cases

Parameters	SBP

	Pearson Correlation	**P. value**
Urea	0.183*	0.037
Creatinine	0.097	0.271
Uric acid	0.521**	0.000
BUN	0.178*	0.043
BCR	0.170	0.053

As shown by Table (10), the correlation of diastolic blood pressure was significant with urea (P=0.024), BUN (P=0.030), and highly significant with uric acid (P=0.000) and blood urea nitrogen creatinine ratio (P= 0.001). Insignificant correlation was shown between serum creatinine and diastolic blood pressure (P=0.285). Mostafa, et al., (2019), reported high Serum uric acid (p<0.0) and higher mean of (SBP) and (DPB) in the pre-eclamptic than the control (p<0.05).

Table 10. Pearson correlation between diastolic blood pressure with urea, creatinine, uric acid, BUN and BCR

Parameters	**DBP**	
	Pearson Correlation	**P. value**
Urea	0.198*	0.024
Creatinine	0.095	0.285
Uric acid	0.482**	0.000
BUN	0.190*	0.030
BCR	0.277**	0.001

Conclusion

- Plasma uric acid, urea and creatinine were increased in the preeclamptic cases. The BCR was found to be within the normal range in the preeclamptic cases.

References

- Akram Elkhair Noor Eldaem, Salah Ismael, Elfadil ALObeid Omer (2016), Assessment of Preeclampsia Multiple Biomarkers in Sudan, *Laboratory medicine journal* **2***(1):19-30*
- Amir Shakarami, Masoumeh Ghafarzadeh, Fatemeh Yari, Leila Fathi (2020), Association between maternal serum uric acid and preeclampsia, Archives of Physiology and Biochemistry
- Arun Jeyabalan, (2013), Epidemiology of preeclampsia: impact of obesity, *Nutrition Reviews, **71**(1):S18–S25.*
- Bohan Lv, Yan Zhang, Guanghui Yuan, Ruting Gu, Jingyuan Wang, Yujiao Zou , Lili Wei, (2022), Establishment of a nomogram model for predicting adverse outcomes in advanced age pregnant women with preterm preeclampsia. BMC Pregnancy Childbirth 22, 221.
- Duaa Adil Osman a, Aimun A E, Ahmed a b, Salah I. Khairy c, Salah Eldin Abdel Hag Abdel Haleem b, (2021), Clinical Status of Pregnancy-Induced Hypertension and Pre-Eclampsia among Sudanese Women, *International Journal of Pharmaceutical Research*, **33**(62A): 167-176.
- Hidajet Paçarizi, Luljeta Begolli, Shefqet Lulaj, Zana Gafurri(2012), blood urea nitrogen/creatinine index is a predictor of prerena l damage in preeclampsa, Journal of Health Sciences. 2(1) : 61-65
- Hall, D. R., & Conti-Ramsden, F, (2019). Acute kidney injury in pregnancy including renal disease diagnosed in pregnancy. *Best Practice & Research Clinical Obstetrics &Gynaecology*, 57(2019): 47-59
- Hamed S, Khalifa T, Mekal F, Ali M, (2022), Evaluation of Changes in Renal Function of Pregnant Women with Preeclampsia in Al-Jabal Al-Akhdar. AlQalam, *Journal of Medical and Applied Sciences*, **5**(1):56-64.
- Hakimeh Moghaddas Sani, Sepideh Zununi Vahed, Mohammadreza Ardalan, (2019), Preeclampsia: A close look at renal dysfunction, *Biomedicine & Pharmacotherapy* 109: 408–416.
- Ioannis Bellos, Vasilios Pergialiotis, Dimitrios Loutradis, Georgios Daskalakis (2020), The prognostic role of serum uric acid levels in preeclampsia: A meta-analysis, *Journal of Clinical Hypertension* **22**:826–834.
- J.A. Hutcheon Jennifer A. Hutcheon, Sarka Lisonkova, K.S. Joseph, (2011),Epidmoiology Of Pre-Eclampsia And The Other Hypertensive Disorders of Pregnancy Best Practice & Research Clinical Obstetrics And Gynaecology **25**:391–403.
- LA Magee, P von Dadelszen, W Stones, M Mathai, (2016), The FIGO Text book of Pregnancy Hypertension An evidence-based guide to monitoring, prevention and management (xiv- xvi).
- Mark A. Brown, Laura A. Magee, Louise C. Kenny, S. Ananth Karumanchi, Fergus P. McCarthy, Shigeru Saito, David R. Hall, Charlotte E. Warren, Gloria Adoyi, Salisu Ishaku; (2018), Hypertensive Disorders of Pregnancy: ISSHP Classification, Diagnosis, and Management Recommendations for International Practice, *Hypertension*, **72**:24-43.
- Mark W. Cunningham, Jr. and Babbette La Marca, (2018), *Hypertensive Disorders of Pregnancy: Effects on Mother and Baby* Risk of cardiovascular disease, end-stage renal disease, and stroke inpostpartum women and their fetuses after a hypertensive pregnancy, *Am J Physiol Regul Integr Comp Physiol*, 315: 521–528.
- Nan H. Triano, MSN, RNC-OB, NE-BE, C-FM(2018), physiology and hemodynamic changes during pregnancy American Association of Critical care Nurses, *Adv Crit Care* **29** (3): 273-283.

- Neil Baum, M.D. Carmelo C. Dichoso, M.D.C. Eugene Carlton, JR., M.D. 1975, Blood Urea Nitrogen and Serum Creatinine, Physiology and Interpretations, Urology, *Academia.edu* **5**: 583-588.
- OloruntobaAyodeleEkun, Oluwatumininu Mary Olawumi, Christian Chigozie Makwe, NkeirukaOgochukwu Ogidi (2018), Biochemical Assessment of Renal and Liver Function among Preeclamptics in Lagos Metropolis, *international Journal of Reproductive Medicine*, 2018:1-6.
- Opichka, M.A.; Rappelt, M.W.; Gutterman, D.D.; Grobe, J.L.; McIntosh, J.J, 2021 Vascular Dysfunction in Preeclampsia. *Cells*, 10(11), 3055.
- Ranjit S. Ambad, Archana Dhok, (2019), The Role of Serum Urea, Creatinine, Uric Acid in Diagnosis of Pre-Eclampsia and Eclampsia, *International Journal of Medical and Biomedical* Studies, **9**(3):77- 80.
- UV Ukah, B Payne, AM Cote, Z Hoodbhoy, P von Dadelszen (2016), Risk factors and predictors of pre-eclampsia, The FIGO Text book of Pregnancy Hypertension An evidence-based guide to monitoring, prevention and management (2016) 75-100.
- Vikse B E, Irgens L M, Leivestad T, Skjaerven R, Iversen B M, (2008), Preeclampsia and the risk of end-stage renal disease. The *New England Journal of Medicine*, 359: 800–809.
- Hind M. Behheiry ,Ibrahim ,Mazin S Abdalla ,Ahmed M. Sharif, Ahmed M.sharif, Amal M.Saeed (2018),Correlations of complete blood count, liver enzyme and serum uric acid in Sudanese pre-eclamptic cases, *International Journal of Reprodction, Contraception, Obstetrics and Gynecology*, **7** (4) P (1308-1312).