E-ISSN:2455-5444
P-ISSN:2581-4389
RNI:MPENG/2017/74037
Research Article
Protein

Obs Gyne Review - Journal of Obstetric and Gynecology
2021 Volume 7 Number 3 May-June

Publisher
MEDRESEARCH
www.medresearch.in

# Comparative efficacy of protein creatinine ratio and calcium creatinine ratio in determining organ dysfunction in ante-natal patients with pre-eclampsia

**Sah S.[1*], Gupta S.[2], Goel R.[3]**

DOI: https://doi.org/10.17511/joog.2021.i03.01

[1*] Shanti Sah, Associate Professor, Department of Obstetrics and Gynaecology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.

[2] Shipra Gupta, Junior Resident, Department of Obstetrics and Gynaecology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.

[3] Ruchica Goel, IVF Consultant, Department of Obstetrics and Gynaecology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.

**Aim:** To evaluate the biochemical parameters in determining the severity of pre-eclampsia and compare the efficacy between protein creatinine ratio and calcium creatinine ratio in determining organ dysfunction in ante-natal women with pregnancy-induced hypertension. **Material and Methods:** 150 cases of pregnancy-induced hypertension admitted in the labour room were studied in the Department of Obstetrics and Gynaecology, SRMSIMS and were divided into two groups mild and severe pre-eclampsia depending on blood pressure, clinical and biochemical parameters. Various parameters for renal function and liver function were evaluated along with fundoscopy. **Results:** On the evaluation of various parameters of renal function test and liver function test, a statistically significant p-value was observed with increase in grade of pre-eclampsia. When abnormal organ functions were compared, it was observed that PCR ≥ 0.3 is associated with 85%, 75.6% and 81.25% cases of abnormal fundoscopy, deranged renal function test and deranged liver function test compared to CCR ≤ 0.04 which was associated with 77%, 78.6% and 65% cases of abnormal fundoscopy, deranged renal function test and deranged liver function test respectively. **Conclusion:** The degree of derangement among biochemical parameters increases as the disease progresses. Early determination by a single test helps to predict organ involvement and correlates with disease severity.

**Keywords:** Pre-eclampsia, Pregnancy-induced hypertension, Fundoscopy, Renal function test, Liver function test, Protein-creatinine ratio, Calcium-creatinine ratio

**Corresponding Author**

Shanti Sah, Associate Professor, Department of Obstetrics and Gynaecology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.
Email: shantisahmsog@gmail.com

**How to Cite this Article**

Sah S, Gupta S, Goel R. Comparative efficacy of protein creatinine ratio and calcium creatinine ratio in determining organ dysfunction in ante-natal patients with pre-eclampsia. Obs Gyne Review J Obstet Gynecol. 2021;7(3):28-34.
Available From
https://obstetrics.medresearch.in/index.php/joog/article/view/136

**To Browse**

| Manuscript Received | Review Round 1 | Review Round 2 | Review Round 3 | Accepted |
|---|---|---|---|---|
| 2021-05-11 | 2021-05-22 | 2021-05-28 | 2021-06-08 | 2021-06-16 |

| Conflict of Interest | Funding | Ethical Approval | Plagiarism X-checker | Note |
|---|---|---|---|---|
| No | Nil | Yes | 7% | |

# Introduction

Hypertensive disorder of pregnancy accounts for the third most common cause of maternal mortality after haemorrhage and sepsis. The incidence of pre-eclampsia is around 5-10% of all pregnancies and contributes to 14-16% of maternal mortality worldwide [1]. Pre-eclampsia is a multisystem disorder associated with a rise in blood pressure after the 20th week of gestation. Pre-eclampsia can be classified as mild – when no other associated symptoms are present or severe- when associated with neurological disturbance (headache, visual disturbance, exaggerated tendon reflex, convulsion), hematological disturbance (thrombocytopenia, DIC, hemolysis), liver affection ( elevated liver enzyme, upper abdominal pain, subcapsular hematoma), renal insufficiency (reduced urinary volume, raised serum creatinine, increased protein excretion) and disturbance in bone mineral metabolism [2]. The above effect leads to an increase in maternal and perinatal morbidity. Hence, we tried to assess the extent of organ involvement with the rise in blood pressure and biochemical predictors which would reliably assess the severity of disease, thereby helping in management and improving the prognosis. Various biochemical markers have been evaluated for the prediction of pre-eclampsia based on the pathophysiology of the disease. Spot urinary protein-creatinine ratio is one of the variables shown to be sufficient to assess proteinuria in the diagnosis of pre-eclampsia compared to the 24-hour value and a ratio > 0.3 mg/dl has been shown to meet or exceed 300 mg protein in 24-hour urinary collection [3]. Another parameter is decreased in urinary calcium-creatinine ratio. As pregnancy constitutes increased calcium requirement which is compensated by physiological increased absorption, which lacks in patients at risk of pre-eclampsia, thus there is a decline in urinary calcium excretion and hence results in the abnormal urinary calcium-creatinine ratio [4]. Thus, we also tried to find out a better biochemical predictor which can detect the pathological changes of pre-eclampsia more reliably.

# Material and Methods

We did a prospective case study conducted in the Department of Obstetrics and Gynaecology over 1.5 years from November 2018 to May 2020.

**Inclusion criteria:** Patients with a singleton pregnancy of ≥ 20 weeks who were previously Normotensive and non-proteinuric with systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mm Hg on two occasions at least 4 hours apart were enrolled.

**Exclusion criteria:**

01. History of chronic hypertension and proteinuria before conception or development of hypertension before 20 weeks of gestation.
02. Patients with chronic renal disease.
03. Patients with a history of recurrent urinary tract infections.
04. Molar pregnancy.
05. Multiple pregnancies.
06. Patients with associated liver dysfunction.
07. Patients who delivered before completion of collection of 24- hour urine sample.

Ethical clearance was obtained from the Institutional ethical committee. 150 cases were recruited and grouped as mild and severe pre-eclampsia based on blood pressure and clinical parameters. Their biochemical parameters for renal and liver function were assessed. Spot urinary protein- creatinine ratio in all patients with a cutoff value of 0.3. The validity of PCR (taken as Group 1) was compared to a previous study conducted on 50 pre-eclamptic women where organ involvement was studied based on the calcium-creatinine ratio (taken as Group 2) with a cutoff value of 0.04. Both the groups were compared concerning the percentage of pre-eclamptic patients showing organ involvement in terms of abnormal fundoscopy, renal and liver function test and the results were analyzed on software IBM SPSS version 20.0. We also aimed to determine PCR versus CCR to predict the severity of pre-eclampsia.

# Results

Recruitment of patients in both groups was matched according to age, parity, SES and BMI.

**Table 1: Clinical and biochemical parameters of both groups**

| GROUPS | SYSTOLIC BP (mmHg) | DIASTOLIC BP (mmHg) | URINARY CREATININE (mg/dl) | URINARY CALCIUM (mg/dl) | URINARY PROTEIN (mg/dl) |
|---|---|---|---|---|---|
| Group 1 (PCR) | 155.59±2.48 | 99.7±0.2 | 85.74±22.53 | - | 87.99±50.8 |
| Group 2 (CCR) | 150.44±10.68 | 95.96±7.35 | 83.41±58.60 | 4.03±5.74 | - |

The mean systolic and diastolic BP among both groups were the same. No significant difference was observed in urinary creatinine levels among both groups.

Mean urinary protein was estimated in group 1 which was 87.99±50.8 mg/dl while mean urinary calcium was estimated in group 2 which was 4.03±5.74 mg/dl.

**Table 2: Relationship of the severity of PIH with abnormal liver and renal function test among patients of group 1**

| Biochemical parameters | Mild PE (n= 24) | | Severe PE (n= 72) | | P value |
|---|---|---|---|---|---|
| LFT | Mean | (±) SD | Mean | (±) SD | |
| S. Bilirubin (mg/dl) | 1.01 | ± 0.07 | 1.47 | ±1.26 | 0.003 |
| Total mean (mg/dl) | 1.24 | | | | |
| (±) SD | ±0.84 | | | | |
| SGOT (IU/L) | 52.3 | ±16.33 | 129 | ±88.7 | 0.000 |
| Total mean (IU/L) | 90.65 | | | | |
| (±) SD | ±51.17 | | | | |
| SGPT (IU/L) | 51.69 | ±25.40 | 119 | ±75.6 | 0.000 |
| Total mean (IU/L) | 85.34 | | | | |
| (±) SD | ±35.4 | | | | |
| S. ALP (IU/L) | 199.91 | ±47.34 | 387.92 | ±181.0 | 0.000 |
| Total mean (IU/L) | 293.92 | | | | |
| (±) SD | ±94.51 | | | | |
| RFT | Mild PE (n = 51) | | Severe PE (n = 7) | | |
| S. Urea (mg/dl) | 18.94 | ±6.46 | 40.44 | ±24.44 | 0.00002 |
| Total mean (mg/dl) | 29.69 | | | | |
| ( ±) SD | ±12.71 | | | | |
| S. Creatinine (mg/dl) | 0.62 | ±0.59 | 1.06 | ±0.61 | 0.00001 |
| Total mean (mg/dl) | 0.84 | | | | |
| ( ±) SD | ±0.01 | | | | |
| S. Uric acid (mg/dl) | 2.64 | ±1.98 | 7.77 | ±2.64 | 0.00002 |
| Total mean (mg/dl) | 5.21 | | | | |
| ( ±) SD | ±0.47 | | | | |

Out of 150 cases of pre-eclampsia (PE), 96 cases had deranged LFT while 127 cases had deranged RFT.

A statistically significant change in all the parameters was observed among mild and severe pre-eclampsia.

**Table-3: Organ involvement according to the severity of PIH in both groups**

| Organ System | Group 1 (n=150) PCR | | | | Group 2 (n=50) CCR | | | |
|---|---|---|---|---|---|---|---|---|
| | Mild (72) | | Severe (78) | | Mild (27) | | Severe (23) | |
| | Normal | Deranged | Normal | Deranged | Normal | Deranged | Normal | Deranged |
| LFT | 48 (88.9%) | 24 (25%) | 6 (11.1%) | 72 (75%) | 21 (70%) | 6 (30%) | 9 (30%) | 14 (70%) |
| RFT | 21 (91.3%) | 51 (40.2%) | 2 (8.7%) | 76 (59.8%) | 22 (61.1%) | 5 (35.7%) | 14 (38.9%) | 9 (64.3%) |
| Fundus | 68 (55.3%) | 4 (14.8%) | 55 (44.7%) | 23 (85.2%) | 25 (67.6%) | 2 (15.4%) | 12 (32.4%) | 11 (84.6%) |

Of total deranged LFT, RFT and fundus in Group 1- 25%, 40.2% and 14.8% were of mild pre-eclampsia and 75%, 59.8% and 85.2% were of severe pre-eclampsia which was indifferent to total deranged organ function in Group 2 i.e. 30%, 35.7% and 15.4% in mild cases and 70%, 64.3% and 84.6% in severe cases respectively. The p-value between the deranged organ function in both groups were 0.642, 0.747 and 0.964 for LFT, RFT and fundus respectively.

**Table 4: Comparison of specific organ insult among both groups.**

| Biochemical variables | | Abnormal organ function (%) | | |
|---|---|---|---|---|
| Groups | Cut off | Fundus | RFT | LFT |
| PCR (Group 1) | < 0.3 | 4 (14.8 %) | 31 (24.4%) | 18 (18.7%) |
| | ≥ 0.3 | 23 (85.2%) | 96 (75.6%) | 78 (81.25%) |
| CCR (Group 2) | ≤ 0.04 | 10(77%) | 11 (78.6%) | 13(65%) |
| | > 0.04 | 3 (23%) | 3 (21.4%) | 7 (35%) |

Percentage derangement in renal function was comparable in both groups with a cutoff value of ≥ 0.3 for PCR and ≤ 0.04 for CCR, while a significant more case of abnormal Fundus and liver function was detected with PCR ≥ 0.3.

**Table 5: Statistical analysis of cut off value in both groups**

| | Cut off | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|
| Group 1 – PCR | ≥ 0.3 | 51.39% | 92.3% | 86.05% | 67.29% |
| Group 2- CCR | ≤ 0.04 | 52% | 86% | 79% | 64% |

Specificity and PPV of PCR were more compared to CCR to determine organ dysfunction. The cut of our study was taken as a standard cut off based on various other studies.

# Discussion

Organ involvement directly correlates with the severity of pre-eclampsia. In normal pregnancy, systemic vascular resistance falls and the blood flow increases. Relaxin, a peptide hormone produced by the corpus luteum, decidua and placenta plays an important role in the regulation of hemodynamics stimulating the formation of endothelin, which in turn mediates vasodilatation of renal arteries via nitric oxide synthesis which counterbalances the vasoconstrictive effect of the rennin-angiotensin-aldosterone system [5]. In pre-eclampsia, there is a failure of trophoblast uterine interaction causing stress in syncytiotrophoblast leading to systemic inflammatory response resulting from disruption of hemostatic function [6]. This leads to profound vasoconstriction affecting all organ systems and endothelial damage and dysfunction.

In our study, mean bilirubin was 1.01 ± 0.07 and 1.47 ± 1.26 mg/dl in mild and severe pre-eclampsia respectively. Mean SGOT and SGPT in mild and severe pre-eclampsia was 52.3 ± 16.33 IU/L / 51.69 ± 25.4 IU/L and 129.0 ± 88.7 IU/L / 119 ± 75.6 IU/L respectively. Our observations were statistically significant. A similar finding was observed by a study conducted by Kasraeian et al (2018) with mean bilirubin of 0.6 ±0.22 mg/dl and 0.6 ± 0.18 mg/dl, SGOT of 32.45 ± 50.8 IU/L and 43.54 ± 73.63 IU/L and SGPT of 18.78 ± 30.38 IU/L and 32.99 ± 54.07 IU/L for mild and severe pre-eclampsia respectively [7]. Our finding was in contrast to Kasraeian et al in respect to serum alkaline phosphatase. In our study, Alkaline phosphatase among mild and severe pre-eclampsia was 199.91 ± 47.34 IU/L and 387.92 ± 181.0 IU/L respectively compared to 333.94 ± 120.61 IU/L and 321.42 ± 147.74 IU/L according to Kasraeian et al study [7].

In normal pregnancy renal blood flow and GFR increase, both serum urea and creatinine concentration decreases. In pre-eclampsia, renal affection occurs more commonly associated with 20% decreased renal perfusion causing a 32% decrease in glomerular filtration and tubular reabsorption as a result of vasoconstriction and endothelial damage resulting in a change in renal function.

This leads to an increase in serum urea, creatinine and uric acid with decrease urinary creatinine levels compared to normotensive patients, decrease in tubular reabsorption due to glomerular endothelial dysfunction causes increase protein excretion and decrease reabsorption[8]. Urinary calcium excretion also decreases in pre-eclampsia due to increase tubular reabsorption of calcium rather than decreased GFR [8]. Pre-eclamptic may also have a lower level of urinary calcium excretion with a lower level of 1, 25 D3 [9].

Hypertensive women have higher plasma parathyroid hormone and lower 1,25 Dihydoxy Vit D, hence Vit D insufficiency associated with a change in urinary calcium excretion [10]. Ray et al reported higher basal intracellular free calcium concentration in pre-eclampsia with decrease calcium dependant ATPase activity of erythrocyte and hypocalciuria [11]. In pre-eclampsia, angiogenic imbalance causes an increase in podocytes and increased level of soluble receptor fms like tyrosine kinase 1 (sFlt-1) and reduced concentration of free VEGF leading to glomerular endothelial damage and break infiltration barrier leading to proteinuria [12].

In our study we observed various renal parameters which were significantly increased among increasing grades of pre-eclampsia. The mean S. urea among mild and severe pre-eclampsia was 18.94 ± 6.46 mg/dl and 40.44 ± 24.44 mg/dl, S. creatinine was 0.62 ± 0.59 mg/dl and 1.06 ± 0.61 mg/dl and S.

Uric acid were 2.64 ± 1.98 mg/dl and 7.77 ± 2.64 mg/dl respectively which were statistically significant. Our findings were following the finding of Hazare et al and Kasraeian et al where mean S. creatinine among mild preeclampsia was 0.75 ± 0.23 mg/dl and 0.84 ± 0.27 mg/dl whereas in severe pre-eclampsia was 1.3 ± 0.19 mg /dl and 0.9 ± 0.26 mg/dl respectively [13,7].

As renal function deteriorates the volume of protein excretion increases and creatinine clearance decreases, hence protein creatinine ratio (PCR) helps in predicting the severity of the disease. In our study a cut off value of 0.3 was taken and was observed that about 85.2 %, 75.6% and 81.25 % of abnormal finding in the fundus, renal function and liver function had PCR ≥ 0.3. Our study was inconsistent with to study of Gaddy Dufac et al where the cut off value of ≥ 0.3 was 85 % specific in predicting diseases severity while Kumari et al observed 84 % specificity and 90 % sensitivity with a cut off value of ≥ 0.3 [14,15].

It has also been observed that with increasing tubular damage as the disease progresses fractional excretion of calcium is reduced hence measuring calcium to creatinine ratio (CCR) also helps in predicting disease severity. CCR cut off value of 0.04 in our study showed 77 %, 78.6% and 65 % cases of abnormal fundoscopy, renal and liver function test had a value ≤ of 0.04. Our findings were similar to the observation of Sinha R et al and Prasad et al where 81.25 % and 89 % cases respectively of pre-eclampsia had CCR cut off value ≤ 0.04 [16,17].

In our study both groups had a similar incidence of abnormality in renal function with PCR ≥ 0.3 and CCR ≤0.04. The sensitivity of both groups was similar in our study however, the specificity and positive predictive value for PCR were found superior to CCR. Similar to our finding Rizk et al stated that area under ROC curve to predict proteinuria was 0.82 (95 % confidence interval 0.73 to 0.92, p < 0.001) for protein creatinine and 0.55 (95 % confidence interval 0.43 to 0.68, p = 0.2) for calcium creatinine[18]. Similarly, Ibrahini et al found that role of calcium creatinine ratio in urine is inferior to proteinuria in predicting pre-eclampsia [19].

Contrary to our finding Lekha et al concluded that CCR is 94 % specific with a sensitivity of 66%, PPV of 54 % and NPV of 97% compared to microalbuminuria which was 89% specific, 56% Sensitive and PPV of 36 %, the area under the curve for CCR was higher (0.908) when compared to microalbuminuria (0.873) and S. uric acid (0.799) [20] Begum et al also concluded a positive correlation between urinary calcium/ creatinine ratio and urinary calcium (r = +0.68, p< 0.001) but a negative correlation (r = -0.39, p < 0.001) noted between urinary calcium/creatinine and urinary protein, CCR decreases in pre-eclampsia hence CCR can be regarded as a predictor for pre-eclampsia [21].

# Conclusion

This study shows that a high absolute magnitude of liver and renal function test as well as fundoscopic findings are useful means to predict disease severity. However, if a single biochemical test is required our finding for both protein creatinine ratio and calcium creatinine ratio in assessing disease severity is approx 50 % sensitive. But our was a small study with a limitation of unequal sample size a larger randomized study is yet needed to determine a better single biochemical test to ascertain disease severity.

# What does this study add to existing knowledge?

Protein-creatinine ratio and Calcium-creatinine ratio, both of these biochemical parameters can be used as the substitute for 24 hours urinary protein collection with equal sensitivity for early detection of pre-eclampsia. However, the protein-creatinine ratio is more specific compared to the calcium-creatinine ratio if a single biochemical test is required.

# Acknowledgement

I thank my Dr Shipra Gupta for helping me in patient recruitment and data collection and Dr Ruchica Goel in compiling the data.

# Reference

01. Gemechu KS, Assefa N, Mengistie B. Prevalence of hypertensive disorders of pregnancy and pregnancy outcomes in Sub-Saharan Africa- A systematic review and meta-analysis. Womens Health (Lond). 2020 Jan-Dec;16;1745506520973105. *doi: 10.1177/1745506520973105 [Crossref][PubMed] [Google Scholar]*

02. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No 203- Chronic Hypertension in Pregnancy. Obstet Gynecol. 2019 Jan;133(1)e26-e50. *doi: 10.1097/AOG.0000000000003020 [Crossref] [PubMed][Google Scholar]*

03. Wheeler TL 2nd, Blackhurst DW, Dellinger EH, Ramsey PS. Usage of spot urine protein to creatinine ratios in the evaluation of preeclampsia. Am J Obstet Gynecol. 2007 May;196(5)465;e1-4. *doi: 10.1016/j.ajog.2006.10.892 [Crossref] [PubMed][Google Scholar]*

04. Khandelwal, Smriti, Surekha Tayade, and Chetan Gode. "Prediction of Pre-Eclampsia by Urinary Calcium and Creatinine Ratio". International Journal of Current Research and Review. 12(2020)19-22. *[Crossref][PubMed][Google Scholar]*

05. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc J Afr. 2016 Mar-Apr;27(2)89-94. *doi: 10.5830/CVJA-2016-021 [Crossref][PubMed] [Google Scholar]*

06. Burton GJ, Redman CW, Roberts JM, Moffett A. Pre-eclampsia- pathophysiology and clinical implications. BMJ. 2019 Jul 15;366;l2381. *doi: 10.1136/bmj.l2381 [Crossref][PubMed][Google Scholar]*

07. Kasraeian M, Asadi N, Vafaei H, Zamanpour T, Shahraki HR, Bazrafshan K. Evaluation of serum biomarkers for detection of preeclampsia severity in pregnant women. Pak J Med Sci. 2018 Jul-Aug;34(4)869-873. *doi: 10.12669/pjms.344.14393 [Crossref][PubMed][Google Scholar]*

08. Al-Malt A M, Petrulis A S, Amini S B, Mann L I. Hypocalciuria can differentiate preeclampsia from chronic hypertension in the third trimester. Journal of Maternal-Fetal Medicine. 2;6(1993)300-304. *[Crossref][PubMed][Google Scholar]*

10. Hojo M, P August. "Calcium Metabolism in Preeclampsia- Supplementation May Help". Medscape women's health. 2;1(1997)5-5. *[Crossref] [PubMed][Google Scholar]*

11. Tsuda K. Calcium metabolism and its relation to blood pressure during pregnancy. Am J Hypertens. 2015 Feb;28(2)283. *doi: 10.1093/ajh/hpu207 [Crossref][PubMed][Google Scholar]*

12. Ray J, Vasishta K, Kaur S, Majumdar S, Sawhney H. Calcium metabolism in pre-eclampsia. Int J Gynaecol Obstet. 1999 Sep;66(3)245-50. *doi: 10.1016/s0020-7292(99)00096-x [Crossref] [PubMed][Google Scholar]*

13. Fishel Bartal M, Lindheimer MD, Sibai BM. Proteinuria during pregnancy- definition, pathophysiology, methodology, and clinical significance. Am J Obstet Gynecol. 2020 Sep 1;S0002-9378(20)30989-3. *doi: 10.1016/j.ajog. 2020.08.108 [Crossref][PubMed][Google Scholar]*

14. Hazari N R, Hatolkar V S, Munde S M. "Study of serum hepatic enzymes in preeclampsia". International Journal of Current Medical and Applied Sciences. 2;1(2014)1-8. *[Crossref][PubMed][Google Scholar]*

15. Ladson Gaddy-Dubac M D, et al. "Spot Urine Protein- Creatinine Ratio versus 24-hour Urine Total Protein to Screen for Preeclampsia". MAHEC Online Journal of Research. 1(1)1-7. *[Crossref][PubMed] [Google Scholar]*

16. Kumari A, Singh A, Singh R. Evaluation of rapid diagnostic methods of urinary protein estimation in patients of preeclampsia of advanced gestational age. J Obstet Gynaecol India. 2013 Oct;63(5)306-10. *doi: 10.1007/s13224-012-0343-5 [Crossref] [PubMed][Google Scholar]*

17. Sinha, Rashmi, and Indu Bhushan. "Study of urinary Calcium/Creatinine Ratio (CCR) in a spot sample of urine for early prediction of preeclampsia". IOSR Journal of Dental and Medical Sciences. 15;5(2016)101-104. *[Crossref][PubMed] [Google Scholar]*

18. Prasad I, Kumari B, Roy AN, Prakash P. National Evaluation of urinary calcium creatinine ratio in pre – eclampsia. Journal of Laborartory Medicine. 2016 April;5(2)1-5. *doi: 10.7860/NJLM/2016/17110:2102 [Crossref][PubMed][Google Scholar]*

19. Rizk D E E, et al. "Predicting proteinuria in hypertensive pregnancies with urinary protein-creatinine or calcium-creatinine ratio". Journal of perinatology. 27;5(2007)272-277. *[Crossref] [PubMed][Google Scholar]*

20. Ibrahimi L, Paçarada M, Latifi Hoxha S, Bimbashi A, Ademi Ibishi V. Role of Calcium/Creatinine Ratio in Urine Compared with Proteinuria and Uric Acid in Predicting Preeclampsia- A Study from Kosovo. Med Sci Monit Basic Res. 2021 Mar 1;27;e929845. *[Crossref][PubMed][Google Scholar]*

21. Lekha Tejaswi Y, Preethi BP. Estimation of serum uric acid, urinary calcium–creatinine ratio and microalbuminuria in prediction of pre- eclampsia. Int Journal of clinical biochemistry and research. Apr-Jun,2018;5(2)277–283. *Doi: 10.18231/2394-6377.2018.0057 [Crossref][PubMed][Google Scholar]*

22. Begum H, Rahman M N, Ferdous M, Basak S K, Yasmin N, Parveen A. Evaluation of Spot Urinary Calcium to Creatinine Ratio in Preeclampsia- A Cross Sectional Comparative Study. Journal of National Institute of Neurosciences Bangladesh. 3;1(2017)14-20. *[Crossref][PubMed][Google Scholar]*