Evaluation of Urinary Calcium, Creatinine and their Ratio in Preeclampsia: A Case-control Study

SONIA JINDAL[1], SUNITA MANHAS[2], MONIKA RATHEE[3]

ABSTRACT

Introduction: Preeclampsia is a hypertensive disorder characterised by high blood pressure during pregnancy. It is the major cause of maternal and perinatal morbidity and mortality in females. Prediction of Pregnancy Induced Hypertension (PIH) can be done by using a valuable marker i.e. Urinary Calcium-Creatinine ratio (UCa/Cr).

Aim: To evaluate the urinary calcium, creatinine and UCa/Cr ratio in patients with preeclampsia and also to check the association of UCa/Cr ratio with the severity of the disease.

Materials and Methods: The present case-control study was conducted in the Department of Biochemistry in collaboration with department of Obsteritics and Gynaecology, Maharishi Markandeshwar University, Ambala, Haryana, India from January 2018 to January 2021. Total of 120 pregnant women with gestational age ≥20 weeks (60 normal and 60 preeclampsia) were evaluated for

urinary calcium, urinary creatinine and UCa/Cr ratio. For statistical analysis, unpaired t-test and Chi-square test and was applied.

Results: The mean age of control group was 27.51±5.05 years and for case group was 29.8±5.49 years. The level of urinary calcium and urinary creatinine was found to be significantly (p-value <0.001) lower in case group (3.54 mg/dL and 42.90 mg/dL, respectively) as compared to control group (8.22 mg/dL and 80.40 mg/dL, respectively). The level of UCa/Cr ratio was also significantly (p-value <0.001) lower in case group (0.08±0.04) than control group (0.11±0.04) (p<0.001).

Conclusion: The UCa/Cr ratio was significantly decreased in preeclampsia compared to normal pregnancy. UCa/Cr ratio in spot urine can be useful in identifying pregnant women at risk for preeclampsia.

INTRODUCTION

Preeclampsia is most common hypertensive disorder accounting for approximately 2-10% of the total gestations [1,2]. PIH is a major cause of maternal and perinatal morbidity and mortality in females [3]. About 5-7 % of the pregnancies are affected by preeclampsia and hypertensive disorders [4]. Prediction of preeclampsia in patients extremely essential to save mother and foetal life so that early detection and timely intervention and treatment will prevent the occurrence of complications of PIH [5,6]. The pathophysiology behind preeclampsia is decreased perfusion of organs due to vasospasm. It is usually associated with oedema or proteinuria or both. The mechanism is unknown till now that how pregnancy initiates or aggravates hypertension. It is one of the most significant unsolved problems in Obstetrics. This is the disorder of widespread vascular endothelial malfunction and vasospasm which occurs after 20 weeks of gestation and presents till 4-6 weeks postpartum [7].

Prediction of PIH can be done by using UCa/Cr [8]. In normal pregnancy, there is increase in glomerular filtration rate which results in increasing of creatinine clearance and calcium excretion in urine. But in women developing Pulmonary Embolisms (PE) because of vasospasm and decrease of renal flow, creatinine clearance decreases, followed by increase in serum creatinine level [9].

The conditions like eclampsia, preeclampsia and gestational hypertension are mostly preventable [10]. This has led to the screening of the deliberate examination of substantial segments of the population in search for the disease at its earlier stages, is a logical extension of the role of preventive medicine [11]. The pregnant women who are at risk for preeclampsia can be identified by proposing various methods. Renal function changes in preeclampsia indicate that some of the changes are present before the clinical diagnosis of preeclampsia. The association of microalbuminuria and hypocalciuria with preeclampsia as early as 24 weeks is one of the changes [12].

Various predictors like roll-over test, second trimester mean arterial pressure test, serum uric acid test, angiotensinogen sensitivity test, isometric test have been used for prediction of gestational hypertension. But because of their complexity in result interpretation or high incidence of false positivity these are not proved ideal [7]. It has been found that decreased urinary excretion of calcium and creatinine may be considered as a useful tool for the early diagnosis of preeclampsia [7]. When used as a single test, the UCa/Cr ratio is a better predictor of preeclampsia than the urinary microalbuminuria concentration [13]. Inspite of great advances in Obstetrics, this disorder is very much common in India.

Punthumapol C and Kittichotpanich B in their study found increased serum uric acid levels which were independently and significantly associated with severity of preeclampsia [14]. Hawkins TLA et al., studied that the influence of the uric acid levels has major adverse effects on maternal and particularly in foetal. They depicted that, hyperuricaemia remains important finding as it identifies women at increased risk of adverse outcomes and even in women with gestational hypertension without any other feature of preeclampsia [15].

Therefore, the study aimed to determine the relationship between hypocalciuria, preeclampsia, and calcium to creatinine ratio for early detection of preeclampsia in a random urine sample which may be an effective tool and it may identify population of greatest risk to be included in primary prevention programmes.

MATERIALS AND METHODS

The present case-control study was conducted in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynaecology, Maharishi Markandeshwar University, Ambala, Haryana, India, from January 2018 to January 2021. Ethical clearance was taken from Institutional Ethics Committee (No. 1619). Consent forms were obtained from every participant after explaining the study purpose.

Inclusion and exclusion criteria were selected according to the previous study done by Vasava S et al., [16].

Inclusion criteria: Pregnant women at 20 or more weeks of gestation with Systolic Blood Pressure (SBP) ≥140 mmHg or Diastolic Blood Pressure (DBP) ≥90 mmHg [16] along with proteinuria- (>5 g/24 hour), impaired liver function, singleton primigravida, thrombocytopenia, pulmonary oedema, oliguria- <500 mL/24 hour was included as cases [17]. Normotensive pregnant women with gestational age ≥20 weeks and without proteinuria, oliguria was included.

Exclusion criteria: The subjects with history of rheumatoid arthritis, renal disorder, cardiovascular disease/gestational diabetes mellitus, smoking, multiple pregnancy, stroke, any vaginal bleeding, anaemia, chronic hypertension or with any recent or present fever or infectious disease and who are not willing to participate were excluded from the study.

Sample size calculation: The sample size of 120 was calculated at power of 80% at 95% of confidence.

Total 120 subjects were divided into 2 groups:

Group 1 (case group): 60 pregnant women with preeclampsia were included in group 1, which was further divided according to the severity of preeclampsia into-

- Group 1.1 (Mild preeclampsia) having SBP 140-149 and DBP 90-99 mmHg,
- Group 1.2 (Moderate preeclampsia): SBP 150-159 and DBP 100-109 mmHg and
- Group 1.3 (Severe preeclampsia): SBP ≥160 and DBP ≥110 mmHg [16]. Each divided group includes 20 pregnant women.

Group 2 (control group): 60 normal pregnant women with normal blood pressure were considered as controls.

Study Procedure

Urine sample (5 mL) was collected in sterile urine container. All the samples were analysed on fully auto analyser (Mindray). Urinary calcium was evaluated by Modified Arsenaso method and urinary creatinine by Modified Jaffe's Kinetic method.

Biological reference interval: A normal biological reference value for urinary calcium is 0.8-30 mg/dL, for urinary creatinine is 28-259 mg/dL and for urinary calcium creatinine ratio is less than 0.14 mg/dL. If value of UCa/Cr ratio is more than 0.20, it is the indication of hypercalciuria [18].

STATISTICAL ANALYSIS

The Statistical Package for Social Sciences software (SPSS) version 27.0 is used for statistical analysis. Unpaired t-test and Chi-square test was applied to statistically analyse the data. A p-value <0.05 was considered to be significant.

RESULTS

In the present study the mean age of control group is 27.51±5.05 years and for case group is 29.8±5.49 years. The mean systolic blood pressure for control group and case group was 127.33±12.74 mmHg and 155.16±13.81 mmHg, respectively while diastolic blood pressure was 80.33±6.88 for control group and 104.33±13.45 for case group [Table/Fig-1].

Parameters	Control group Mean±SD	Case group Mean±SD	p-value
Age (in years)	27.51±5.05	29.8±5.49	0.019
Systolic blood pressure	127.33±12.74	155.16±13.81	<0.001
Diastolic blood pressure	80.33±6.88	104.33±13.45	<0.001

[Table/Fig-1]: Distribution of the studied subjects blood pressure recorded in mmHg.
p-value <0.05 is statitsically significant

Case group had significantly lower (3.54±1.97 mg/dL) urinary calcium level than control group (8.22±2.43 mg/dL) (p-value <0.0001). While, urinary creatinine level was significantly lower in cases (80.40±19.32 mg/dL) as compared to controls (42.90±14.94 mg/dL) (p-value <0.0001). Case group had significantly lower U Ca/Cr ratio (0.08±0.04) than control group (0.11±0.04) (p<0.0001) [Table/Fig-2].

Parameters	Control group Mean±SD	Case group Mean±SD	p-value
Urinary calcium (mg/dL)	8.22±2.43	3.54±1.97	<0.001
Urinary creatinine (mg/dL)	42.90±14.94	80.40±19.32	<0.001
Urinary calcium/Creatinine ratio (mg/dL)	0.11±0.04	0.08±0.04	<0.001

[Table/Fig-2]: Comparison of different parameters between normal pregnancy and preeclampsia cases.
p-value <0.05 is statitsically significant

In mild group, 2 (10%) females were with urinary creatinine less than equal to 28 mg/dL, 18 (90%) females were in the range 28-259 mg/dL. In moderate group, 3 (15%) females were with urinary creatinine less than 28 mg/dL, 17 (85%) females were in the range 28-259 mg/dL. In severe group, 2 (10%) females were with urinary creatinine less than 28 mg/dL, 18 (90%) females were in the range 28-259 mg/dL. But this difference was statistically non significant (p-value=0.851) in preeclampsia cases [Table/Fig-3].

Urinary creatinine (mg/dL)	Preeclampsia (Group 1) n (%)			p-value
	Mild	Moderate	Severe	
<28	2 (10)	3 (15)	2 (10)	
28-259	18 (90)	17 (85)	18 (90)	0.851
Total	20 (100)	20 (100)	20 (100)	

[Table/Fig-3]: Urinary Creatinine level among Preeclampsia.

In groups mild, moderate and severe mean value of urinary calcium was 3.88±2.156 mg/dL, 3.35±1.984 mg/dL and 3.39±1.80 mg/dL (p-value=0.647), respectively and mean value of urinary creatinine was 44.17±15.391 mg/dL, 42.99±15.919 mg/dL and 41.54±14.10 mg/dL (p-value=0.86), respectively [Table/Fig-4].

Parameters	Preeclampsia (Group 1)			p-value
	Mild Mean±SD	Moderate Mean±SD	Severe Mean±SD	
Urinary calcium (mg/dL)	3.88±2.156	3.35±1.984	3.39±1.80	0.647
Urinary creatinine (mg/dL)	44.17±15.391	42.99±15.919	41.54±14.10	0.86
Urinary calcium: Creatinine ratio (mg/dL)	1.85±1.27	2.67±2.21	2.01±1.69	0.30

[Table/Fig-4]: Distribution of different parameters among preeclampsia.

DISCUSSION

Preeclampsia is a condition, which cannot be ascribed by any single cause. Insufficient invasion by trophoblast cells in uterine wall can lead to development of a disease in early pregnancy. To explain the pathophysiology of disease there is no scientific evidence [19]. Various studies concluded that calcium homoeostasis is an important part of foetal and maternal physiology during gestation [20-22]. For the production of endothelial derived releasing factor, a certain calcium level is required which maintains vasodilatation in normal pregnancy. Modification of calcium metabolism has been indicated in pathogenesis of hypertension during pregnancy.

In present study, case group had significantly lower urinary calcium and urinary creatinine level than control group (p-value <0.001). The mean and SD of UCa/Cr was 0.08±0.04 in case group and 0.11±0.04 in control group. Patients in case group had statistically significantly lower UCa/Cr ratio than control group (p-value <0.001). In mild, moderate and severe mean value of urinary calcium was 3.88±2.165 mg/dL, 3.35±1.984 mg/dL and 3.39±1.80 mg/dL (p-value >0.05 mg/dL), respectively. In mild, moderate and severe

mean value of urinary creatinine was 44.17±15.391 mg/dL, 42.99±15.919 mg/dL and 41.54±14.10 mg/dL (p-value >0.05 mg/dL), respectively.

Results of the present study corresponds with the result of studies done by Gaurang K et al., [24], Taufield PA et al., (mean urinary calcium concentration was 313±140 mg/24 hour in normal pregnant women and 42±29 mg/24 hour in preeclamptic women) [25], Segovia BL et al., [26], Ingec M et al., [29], Kazemi AFN et al., [9], Sirohiwal D et al., [30], Donovan A et al., [31], Dasgupta M et al., [32], Sheela CN et al., [33]. Comparison of urinary calcium in preeclamptic patients with the normal pregnant women with previous studies is presented in [Table/Fig-5] [9,23-32].

Study (Author)	Year and place of the study	Control group	Case group	p-value
Present study	Haryana 2021	8.22±2.43 mg/dL	3.54±1.97 mg/dL	<0.001
Kazemi AF et al., [9]	Tabriz, Iran 2010	14.12±5.57 mg/dL	9.93±5.28 mg/dL	<0.007
Mittal S. et al., [23]	Indore, India 2014	9.23±3.49 mg/dL	4.56±1.19 mg/dL	<0.0001
Gaurang K et al., [24]	Chitradurga, Karnataka 2015	26.30±5.24 mg/dL	10.53±3.12 mg/dL	<0.001
Taufield PA et al., [25]	1987	313±140 mg per 24 hours	42±29 mgper 24 hours	<0.0001
Segovia BL et al., [26]	Maxico, 2004	8.22±0.36 mg/dL	8.05±0.22 mg/dL	0.21
Tufan B et al., [27]	Florida, 2000	18.18±1.01 mg/dL	10.03±0.55 mg/dL	<0.001
Halhali A et al., [28]	Maxico, 2007	1.38±0.71 mg/dL	0.62±0.38 mg/dL	<0.0001
Ingec M et al., [29]	Turkey 2006	2.3±0.1	2.2±0.1	NS
Sirohiwal D et al., [30]	Rohtak, Haryana 2009	277.43±60.38 mg/dL	167.23±80.63 mg/dL	<0.001
Donovan A et al., [31]	West Indies, 2009	4.43±0.60 mmol/day	1.70±0.26 mmol/day	<0.05
Dasgupta M et al., [32]	Kolkata, 2008	185.26±107.48 vs 197.22±152.02	271.26±222.77 vs 104.41±63.9	0.001

[Table/Fig-5]: Comparison of mean urinary calcium of present study with other studies between Normal Pregnancy and Preeclampsia cases [9,23-32].

In the results of present study, there is decrease of urinary creatinine in case group but the studies done by Mittal S et al., [23], Kazemi AFN et al., [9] and Moni SY et al., [34] showed increase in urinary creatinine in preeclamptic patients [Table/Fig-6] [9,16,23,24,29].

Study (Author)	Year and place	Control group	Case group	p-value
Present study	Haryana, India, 2021	42.90±14.94 mg/dL	80.40±19.32 mg/dL	<0.0001
Kazemi AFN et al., [9]	Ireland, 2010	109.15±56.42 mg/dL	110.61±11.53 mg/dL	<0.001
Vasava S et al., [16]	Gujarat, India, 2018	103.88±40.817 mg/dL	157.61±53.159 mg/dL	<0.0001
Gaurang K et al., [24]	Chitradurga, Karnataka, India, 2015	83.34±17.49 mg/dL	50.38±7.92 mg/dL	<0.01
Mittal S et al., [23]	Indore, India, 2014	78.14±25.60 mg/dL	98.45±29.72 mg/dL	0.0104
Ingec M et al., [29]	Turkey, 2006	59.7±25.9 mg/dL	75.8±39.1 mg/dL	NS

[Table/Fig-6]: Comparison of mean urinary creatinine ratio of present study with other studies between normal pregnancy and preeclampsia cases [9,16,23,24,29].

Kazemi AFN et al., [9] found significantly lower UCa/Cr ratio i.e. for normal pregnant women 0.155±0.084 mg/dL and for preeclamptic is 0.106±0.077 mg/dL (p-value <0.007) [Table/Fig-7] [9,31,32]. Izumi A et al., found a limited value of calcium creatinine ratio in prediction of preeclampsia [35] [Table/Fig-7].

Study (Author)	Year and place	Control group	Case group	p-value
Present study	Haryana 2022	0.11±0.04 mg/dL	0.08±0.04 mg/dL	<0.001
Kazemi AFN et al., [9]	Ireland 2010	0.155±0.084 mg/dL	0.106±0.077 mg dL	<0.05
Donovan A et al., [31]	Scottland 2009	8.1±0.08 mg/dL	3.06±0.03 mg/dL	<0.05
Dasgupta M et al., [32]	Kolkata, 2008	0.22±0.12 mg/dL	0.26±0.10 mg/dL	<0.05

[Table/Fig-7]: Comparison of mean urinary calcium creatinine ratio of present study with other studies between normal pregnancy and preeclampsia cases [9,31,32].

The present study calculated the predictive value of calcium creatinine ratio. Preeclampsia and gestational hypertension is the significant causes of both foetal and maternal morbidity and mortality.

Limitation(s)

The present study was conducted on a small sample size so, to validate these findings further studies should be done on large sample sizes.

CONCLUSION(S)

Present study, concluded that UCa/Cr ratio, urinary calcium and urinary creatinine excretion was significantly decreased in preeclamptic than normotensive pregnant women. For the early diagnosis of preeclampsia, UCa/Cr ratio in spot urine and a single random UCa/Cr may be an effective tool and it may identify population of greatest risk. Therefore, to significantly reduce the mortality and morbidity in patients of preeclampsia, early therapeutic use of calcium may be advised. For future recommendations, UCa/Cr can be studied among high risk factors (diabetes, renal disease, autoimmune disorder etc.) to measure the chances of developing preeclampsia.

Acknowledgement

REFERENCES

[1] Dutta DC, Konar HDC Dutta's textbook of obstetrics. In: Konar H, editor. 8th ed. New Delhi: JAYPEE The Health Service Publisher; 2013;219-40.

[2] Spencer-Jones J. Make every mother and child count. S Afr Med J. 2005;95(6)382-84.

[3] Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P; Canadian Hypertensive Disorders of Pregnancy Working Group. Hypertension Guideline C: Diagnosis, evaluation and management of the hypertensive disorders of pregnancy: Executive summary. J Obstet Gynaecol Can. 2014;36(5):416-41.

[4] Gaurang K, Basavraj S, Rudrappa G, Sabithabai T. Study of random urinary calcium–creatinine ratio in prediction of preeclampsia. Int J Sci Res Publ. 2015;5(7):01-03.

[5] Gant NF, Chand S, Worley RJ, Whalley PJ, Crosby UD, MacDonald PC. A Clinical test useful for predicting the development of acute hypertension in pregnancy. Am J Obstet Gynecol. 1974;120(1):01-07.

[6] Progress in obstetrics and gynaecology Vol 10; edited by John Stud-Screening tests for Pregnancy induced Hypertension. p.69-86.

[7] Ray J, Vasishta K, Kaur S, Majumdar S, Sawhney H. Calcium metabolism in preeclampsia. Int J Gynaecol Obstet. 1999;66(3):245-50.

[8] Gandevani SB, Banaem LM, Mohamadi B, Moghadam NA, Asghari M. Association of high-sensitivity C-reactive protein serum levels in early pregnancy with the severity of preeclampsia and fetal birth weight. J Perinat Med. 2012;40(6):601-05.

[9] Negad Kazemi AF, Sehhatie F, Sattarzade N, Ebrahimi MM. The predictive value of urinary calcium to creatinine ratio, roll-over test and BMI in early diagnosis of preeclampsia. Res J Biol Sci. 2010;5(2):183-86.

[10] Anai T, Hirota Y, Yoshimatsu J, Oga M, Miyakawa I. Hypo-calciuria in women with preeclampsia. Nihon Sanka Fujinka Gakkai Zasshi. 1992;44(1):28-32.

[11] Atallah AN, Hofmeyr GJ, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2000;(3):CD001059.

[12] Chesley LC, Williams LO. Renal glomerular and tubular function in relation to the preeclampsia. E American. J Obstet Gynaecol. 1945;50:367-75.

[13] Rodriguez MH, Masaki DI, Mestman J, Kumar D, Rude R. Calcium/creatinine ratio and microalbuminuria in the prediction of preeclampsia. Am J Obstet Gynecol. 1988;159(6):1452-55. Doi: 10.1016/0002-9378(88)90573-x.

[14] Punthumapol C, Kittichotpanich B. Serum calcium, magnesium and uric acid in preeclampsia and normal pregnancy. J Med Assoc Thai. 2008;91(7):968-73.

[15] Hawkins TLA, Roberts JM, Mangos GJ, Davis GK, Roberts LM, Brown MA. Plasma uric acid remains a marker of poor outcome in hypertensive pregnancy: A Retrospective cohort study. BJOG. 2012;119(4):484-92.

[16] Vasava S, Maheshwari A, Kayal S, Dholakiya J, Mehta K, Sharma H. A comparative study of high sensitive C-reactive protein (hs-CRP) and urinary calcium/creatinine ratio in normal pregnancy and pregnancy induced hypertension in Gujarat, India. IJBCRR. 2018;22(3):01-08.

[17] Dalgleish DJ. Pre-eclampsia 30/05/05. World Anaesthesia tutorial of the week. UK: Royal Bournemouth and Christchurch Hospitals Trust. Available from: http://www.AnaesthesiaUK.com/WorldAnaesthesia. [Accessed on 06/10/2018].

[18] Foley KF, Boccuzzi L. Urine calcium: Laboratory measurement and clinical utility. Lab Med. 2010;41(11):683-86.

[19] Redman CWG, Sacks GP, Sargent IL. Preeclampsia: An excessive maternal inflammatory response to pregnancy. Am J Obstet Gynecol. 1999;180(2 Pt 1):499-06.

[20] Kar J, Srivastava MRK. Role of urinary calcium/creatinine ratio in prediction of pregnancy induced hypertension. J Obstet Gynecol India. 2002;52(2):39-42.

[21] Vallerie SA, Francoise V, Sandra D. Calciuria and preeclampsia- A case control study. Eur J Obstet Gynecol Reprod Boil. 2006;125(2):193-98.

[22] Vahdat M, Kashanian M, Sariri E, Mehdinia M. Evaluation of the value of calcium to creatinine ratio for predicting of pre-eclampsia. J Matern Fetal Neonatal Med. 2012;25(12):2793-94.

[23] Mittal S, Shaikh MKS, Thakur R, Jain D. Calcium/Creatinine ratio in spot urine sample for early detection of preeclampsia. Journal of Evolution of Medical and Dental Sciences. 2014;3(04):966-71, Doi: 10.14260/jemds/2014/1933.

[24] Gaurang K, Basavraj S, Rudrappa G, Sabithabai T. Study of random urinary calcium-creatinine ratio in prediction of preeclampsia. Int J Sci Res Pub. 2015;5(7):01-03.

[25] Taufield PA, Ales KL, Resnick LM, Druzin ML, Gertner JM, Laragh JH, Hypocalciuria in preeclampsia. N Engl J Med. 1987;316(12):715-18.

[26] Segovia BL, Vega IT, Villarreal EC, Licona NA. Hipocalciuria durante el embarazo como factor de riesgo de preeclampsia [Hypocalciuria during pregnancy as a risk factor of preeclampsia]. Ginecol Obstet Mex. 2004;72:570-74.

[27] Bilgin T, Kultu O, Kimya Y, Küçükkömürcü S, Uncu G. Urine calcium excretion inpreeclampsia. T kin J Obstet Gynecol. 2000;10(1):29-32.

[28] Halhali A, Díaz L, Avila E, Ariza AC, Garabédian M, Larrea F, et al. Decreased fractionalurinary calcium excretion and serum, 1,25-dihydroxyvitamin D and IGF-levels in preeclampsia. J Steroid Biochem Mol Biol. 2007;103(3-5):803-06.

[29] Ingec M, Nazik H, Kadanali S. Urinary calcium excretion in severe preeclampsia and eclampsia. Clin Chem Lab Med. 2006;44(1):51-53.

[30] Sirohiwal D, Dahiya K, Khaneja N. Use of 24-hour urinary protein and calcium for prediction of preeclampsia. Taiwan J Obstet Gynecol. 2009;48(2):113-15.

[31] Donovan A. Hypocalciuria in pre-eclampsia and gestational hypertension due to decreased fractional excretion of calcium. Arch Med Sci. 2009;5(1):80-85.

[32] Dasgupta M, Adhikari S, Sanghmita M. Urinary calcium levels in pre-eclampsia. Indian J Obstet Gynaecol. 2008;58:308-13.

[33] Sheela CN, Beena SR, Mhaskar A. Calcium–creatinine ratio and microalbuminuria in prediction of preeclampsia. J Obstet Gynecol India. 2011;61(1):72-76.

[34] Moni SY, Rashid M, Begum HA, Ara S, Ahmed N. Role of calcium therapy on urinary calcium/creatinine ratio in healthy pregnant women and pre-eclamptic women. Bangladesh J Physiol Pharmacol. 2009;25(1&2):07-09.

[35] Izumi A, Minakami H, Kuwata T, Sato I. Calcium-to creatinine ratio in spot urine samples in early pregnancy and its relation to the development of preeclampsia. Metabolism. 1997;46(10):1107-08.

PARTICULARS OF CONTRIBUTORS:
1. Research Scholar, Department of Biochemistry, Maharishi Markandeshwar Deemed to be University, Ambala, Haryana, India.
2. Associate Professor, Department of Biochemistry, Maharishi Markandeshwar Deemed to be University, Ambala, Haryana, India.
3. Assistant Professor, Department of Anatomy, World College of Medical Sciences and Research, Jhajjar, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Monika Rathee,
Assistant Professor, Department of Anatomy, World College of Medical Sciences and Research, Jhajjar-124103, Haryana, India.
E-mail: monikarathee786@gmail.com

AUTHOR DECLARATION:
• Financial or Other Competing Interests: None
• Was Ethics Committee Approval obtained for this study?   Yes
• Was informed consent obtained from the subjects involved in the study?   Yes
• For any images presented appropriate consent has been obtained from the subjects.   NA