**Accuracy of the calcium-creatinine ratio in spot urine sample in prediction of preeclampsia**

**Background:** Preeclampsia is a pregnancy complication, associated with fetal, and maternal morbidity. There is no established test that fulfills all criteria as a good predictor of preeclmpsia.

**Objectives:** This prospective comparative study designed to evaluate the accuracy of calcium-creatinine ratio (CCR) in spot urine sample in prediction of preeclampsia.

**Introduction:** Preeclampsia is hypertensive disease that occurs after 20 weeks gestation [1]. Preeclampsia is a major cause of fetal, and maternal morbidity [2]. Preeclampsia associated with high risk of preterm labor (PTL), intrauterine growth retardation (IUGR), and perinatal mortality [3].

Preeclampsia occurs in 2-10% of all pregnancies in the world. According to the World Health Organization (WHO), the incidence of preeclampsia is seven-fold greater in developing countries (2.8% of live births) compared with developed countries (0.4%).

Several studies showed variations in the incidence, and prevalence of preeclampsia [4]. The etiology of preeclampsia is still not clearly known, while the risk factors for preeclampsia include nulliparity, family history of preeclampsia, previous preeclampsia, obesity, increased insulin resistance, hyperlipidemia, twin, and molar pregnancies [2].

There is no established test that fulfills all criteria as a good predictor of PET [5]. It has been found that increased urinary albumin, and decreased calcium excretion may be an early marker for preeclampsia [6].

*Kazerooni et al,* concluded that single urine calcium to creatinine ratio may be an effective method for screening women at greatest risk for preeclampsia [7].In addition, *Rodriguez et al,* suggested that urinary calcium/creatinine ratio ≤0.04 may be an early marker and/or useful screening tool in predicting the subsequent development of preeclampsia [8]. So, this prospective comparative study designed to evaluate the accuracy of calcium- creatinine ratio (CCR) in spot urine sample in prediction of preeclampsia.

**Patient and methods:** The study will includewomen between 20-40 years old, attending the ante-natal clinic of Ahmadi hospital for ante-natal care after 20 weeks gestation during the period from January 2018 till December 2018 after informed consent, and approval of the Obstetrics department.

Women <20 years, >40 years age, refused to participate in the study and/or refused to give consent will excluded from the study.

After complete obstetrical history, clinical examination, the necessary investigations will be done to exclude other conditions affecting urinary calcium/creatinine ratio.

As part of the routine follow-up in the ante-natal clinics, the urine sample taken from the pregnant women for urine albumin assessment, will be used for the assessment of the CCR after informed consent.

Urinary calcium, urinary creatinine, and urinary calcium/creatinine ratio will be detected using reagent kits Human, and Trades worth Germany. Calcium will be measured by o-cresolpthelein complexions method, and the creatinine will be measured by alkaline picrate method of Jaffe [9]. Follow–up of the studied women till delivery; women who will develop preeclampsia will constitute the study group, and other normotensive women without preeclampsia will constitute the controls.

Primary outcome measures; the accuracy of calcium-creatinine ratio (CCR) in spot urine sample in prediction of preeclampsia.

Secondary outcome measures: possible risk factors for preeclampsia (nulliparity, previous preeclampsia, obesity, hyperlipidemia, twin, and molar pregnancies), and complications associated with preeclampsia (PTL and/or IUGR)

Preeclampsia defined as the presence of hypertension, and urinary proteins after 20 weeks gestation. Hypertension defined as blood pressure above 160/110 mmHg. Urinary protein defined as the presence of ≥ 300 mg protein in the 24-hour collected urine and/or a positive urine dipstick test.

**Sample size and statistical analysis:** The required sample size was calculated using G Power software version 3.17 for sample size calculation (Heinrich Heine Universität; Düsseldorf; Germany), setting α -error probability at 0.05, power (1- β error probability) at 0.95%, and effective sample size (w) at 0.3. The effective sample includes ≥220 women in two groups (110 in the study group, and 110 controls) needed to produce a statistically acceptable figure.

Collected data will statistically analyzed using Statistical Package for Social Sciences (SPSS); computer software version 20 (Chicago, IL, USA). Chi-square test (x2) for qualitative variables, student (t) test for comparison numerical variables to detect the accuracy of the CCR in spot urine sample in prediction of preeclampsia. The Odds ratio, and the relative risk analysis for detection of the possible risks factors for preeclampsia (nulliparity, previous preeclampsia, obesity, hyperlipidemia, twin, and molar pregnancies), and complications associated with preeclampsia (PTL and/or IUGR)

**References**

[1]. Osungbade KO, Ige OK. Public Health Perspectives of Preeclampsia in Developing Countries: Implication for Health System Strengthening. Journal of Pregnancy. 2011; 1-6. [Google Scholar]

 [2]. Wallis AB, Saftlas AF, Hsia J, Atrash HK. Secular Trends in the Rates of Preeclampsia, Eclampsia, and Gestational Hypertension, United States, 1987-2004. Am J Hypertens. 2008;21(5):521-6. doi: 10.1038/ajh.2008.20. [[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/3743319)]

[3]. [Ananth CV](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ananth%20CV%5BAuthor%5D&cauthor=true&cauthor_uid=20010214), [Basso O](https://www.ncbi.nlm.nih.gov/pubmed/?term=Basso%20O%5BAuthor%5D&cauthor=true&cauthor_uid=20010214). Impact of pregnancy-induced hypertension on stillbirth and neonatal mortality. [Epidemiology.](https://www.ncbi.nlm.nih.gov/pubmed/20010214?access_num=20010214&link_type=MED&dopt=Abstract) 2010;21(1):118-23. doi: 10.1097/EDE.0b013e3181c297af. [[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/3743319)]

[4]. Kooffreh ME, Ekott M, Ekpoudom DO. The prevalence of pre-eclampsia among pregnant women in the University of Calabar Teaching Hospital, Calabar. Saudi J Health Sci. 2014;3 (3):133–6. [[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/3743319)]

[5]. [Redman CW](https://www.ncbi.nlm.nih.gov/pubmed/?term=Redman%20CW%5BAuthor%5D&cauthor=true&cauthor_uid=20331588), [Sargent IL](https://www.ncbi.nlm.nih.gov/pubmed/?term=Sargent%20IL%5BAuthor%5D&cauthor=true&cauthor_uid=20331588). Immunology of pre-eclampsia. [Am J Reprod Immunol.](https://www.ncbi.nlm.nih.gov/pubmed/20331588) 2010;63(6):534-43. doi: 10.1111/j.1600-0897.2010.00831.x. [[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/3743319)]

[6]. Hux YR, Yang Z, Zhonghua F, Chan K. ZZ. Calcium metabolism in preeclampsia. Int J Gynaecol Obstet. 1999; 66(3):245-50. [Google Scholar]

[7]. [Kazerooni T](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kazerooni%20T%5BAuthor%5D&cauthor=true&cauthor_uid=12628529), [Hamze-Nejadi S](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hamze-Nejadi%20S%5BAuthor%5D&cauthor=true&cauthor_uid=12628529). Calcium to creatinine ratio in a spot sample of urine for early prediction of pre-eclampsia. [Int J Gynaecol Obstet.](https://www.ncbi.nlm.nih.gov/pubmed/12628529) 2003;80(3):279-83. doi:10.1016/S0020-7292(02)00382-X. [[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/3743319)]

[8]. [Rodriguez MH](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rodriguez%20MH%5BAuthor%5D&cauthor=true&cauthor_uid=3061296), [Masaki DI](https://www.ncbi.nlm.nih.gov/pubmed/?term=Masaki%20DI%5BAuthor%5D&cauthor=true&cauthor_uid=3061296), [Mestman J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mestman%20J%5BAuthor%5D&cauthor=true&cauthor_uid=3061296), [Kumar D](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kumar%20D%5BAuthor%5D&cauthor=true&cauthor_uid=3061296), [Rude R](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rude%20R%5BAuthor%5D&cauthor=true&cauthor_uid=3061296). Calcium/creatinine ratio and microalbuminuria in the prediction of preeclampsia. [Am J Obstet Gynecol.](https://www.ncbi.nlm.nih.gov/pubmed/3061296) 1988;159(6):1452-5. [[PubMed](https://www.ncbi.nlm.nih.gov/pubmed/3743319)]

[9]. Bulter A.R. Clin Chim Acta; 59:227 cited from verly practical clinical Boichemistry 6th ed. ALAn H.G.OWen lock., 1975:604-8. [Google Scholar]