

# USE OF 24-HOUR URINARY PROTEIN AND CALCIUM FOR PREDICTION OF PREECLAMPSIA

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## SUMMARY

**Objective:** To assess the efficacy of 24-hour urinary protein and calcium for the prediction of preeclampsia.

**Materials and Methods:** Two hundred normotensive women at 20–28 weeks' gestation were enrolled in the study. All women were asked to collect a 24-hour urine sample. Urinary protein and calcium were measured and expressed as milligrams per 24 hours. Sensitivity, specificity and predictive values were calculated for each test, and cutoff values were calculated using receiver operating characteristic curves.

**Results:** Twenty-one of the 200 women developed preeclampsia, including eight who developed severe preeclampsia and 13 who developed mild preeclampsia. Compared with the normotensive women ( $n=179$ ), the hypertensive patients ( $n=21$ ) had significantly lower urinary calcium excretion ( $167.23 \pm 80.63$  mg vs.  $277.43 \pm 60.38$  mg) and higher proteinuria ( $351.14 \pm 41.58$  mg vs.  $296.33 \pm 30.03$  mg).

**Conclusion:** A decrease in 24-hour urinary calcium and increase in protein between 20–28 weeks' gestation are risk factors for preeclampsia. [*Taiwan J Obstet Gynecol* 2009;48(2):113–115]

**Key Words:** 24-hour urinary calcium, 24-hour urinary protein, preeclampsia

## Introduction

Hypertensive disorders complicate pregnancy and form one aspect of the deadly triad, along with hemorrhage and infection, and result in significant maternal morbidity and mortality. Hypertension complicates 10% of all pregnancies [1], and the only known cure or definitive treatment is pregnancy termination. Despite widespread research, the exact nature of the disease is not fully understood. Its progression may be slow, rapid or fulminant. Thus, for effective clinical management, it should always be overdiagnosed in order to prevent eclampsia [2].

A recent report suggested that no single test currently fulfils all the established criteria for a good predictor of hypertensive disorders of pregnancy [3]. We, therefore, carried out a prospective study to assess

the values of 24-hour urinary protein and calcium measurements in predicting preeclampsia.

## Materials and Methods

The study group consisted of 200 pregnant women (age, 18–35 years) attending the outpatient department of the Post-Graduate Institute of Medical Sciences, Rohtak. The women were enrolled at 20–28 weeks' gestation and followed up until delivery. Women with a history of hypertension, diabetes mellitus, renal disease, hemoglobin  $< 8$  g/dL, multiple gestations or urinary tract infection were excluded from the study. Informed consent was obtained from all women.

Routine investigations, along with measurements of blood pressure, weight, 24-hour urinary protein and calcium, were performed at the time of registration. Signs and symptoms of preeclampsia were clinically evaluated at each follow-up visit.

Urinary protein was measured using the biuret method, and calcium was measured using the ortho-cresolphthalein complexone method. The records were reviewed, and results were given as median and range.



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**Table.** Anthropometric, clinical and laboratory characteristics\*

	Normotensive group ( <i>n</i> = 179)	Hypertensive group ( <i>n</i> = 21)	<i>p</i>
Maternal age (yr)	23.13 ± 3.22 (19–35)	23.52 ± 3.66 (19–35)	> 0.05
Gravidity	1.59 ± 0.87 (1–6)	1.7 ± 0.97 (1–5)	> 0.05
Hemoglobin (g/dL)	9.2 ± 4.70	8.90 ± 5.21	> 0.05
Blood glucose (mg/dL)	79.22 ± 8.26	74.26 ± 9.21	> 0.05
Blood urea (mg/dL)	20.20 ± 4.29	21.71 ± 4.70	> 0.05
Serum creatinine (mg/dL)	0.82 ± 0.15	0.84 ± 0.13	> 0.05
Serum uric acid (mg/dL)	3.26 ± 1.2	5.76 ± 2.23	> 0.05
Mean arterial pressure (mmHg)	91.892 ± 6.17	104.88 ± 6.96	< 0.001
24-hour calciuria (mg/24 hour)	277.43 ± 60.38 (126–392)	167.23 ± 80.63 (80–340)	< 0.001
24-hour proteinuria (mg/24 hour)	296.33 ± 30.03 (260–460)	351.14 ± 41.58 (260–450)	< 0.05

\*Data are presented as mean ± standard deviation, or mean ± standard deviation (range).

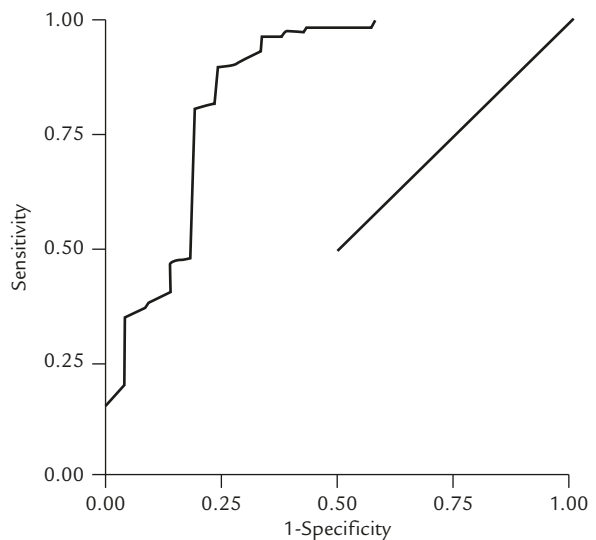
The best cutoff point was established by analyzing the receiver operating characteristic (ROC) curves. Sensitivity, specificity, and positive and negative predictive values were calculated.

## Results

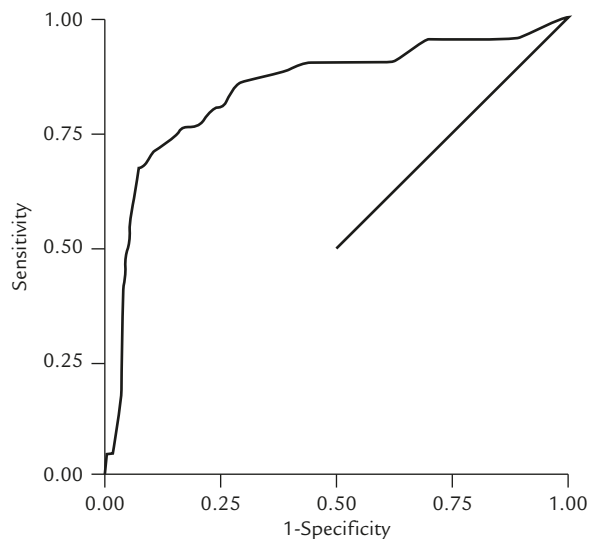
The present study population comprised 200 normotensive, pregnant women (at 20–28 weeks' gestation). Twenty-one women (10.5%) who developed preeclampsia were included in the study group, and those who remained normotensive (89.5%) were used as controls. There were no statistically significant differences in age and parity between the two groups.

Of the patients who developed preeclampsia (*n* = 21), 62% were primigravida, compared with only 54% of the control group. The clinical and laboratory characteristics of the subjects are shown in the Table. The mean value of 24-hour urinary calcium in the hypertensive group was 167.23 ± 80.63 mg (range, 80–340 mg), and that of the control group was 277.43 ± 60.38 mg (range, 126–392 mg). The mean value of 24-hour protein was 351.14 ± 41.58 mg (range, 200–450 mg) in the hypertensive group and 296.33 ± 30.03 mg (range, 260–460 mg) in the control group. The 24-hour urinary calcium was reduced (*p* < 0.01) and 24-hour urinary protein was increased (*p* < 0.05) in those with preeclampsia, compared with the control group. The best cutoff point for identifying the risk of complications was obtained by analyzing the ROC curves for 24-hour urinary calcium and protein.

The ROC curves are shown in Figures 1 and 2. The diagnostic performance of the measurements was expressed as areas under the curves, those of which for calcium and protein were 0.854 and 0.846, respectively. Sensitivity and specificity for the threshold of



**Figure 1.** Receiver operating characteristic curve showing 24-hour urinary calcium.



**Figure 2.** Receiver operating characteristic curve showing 24-hour urinary protein.

220 mg/24-hour urine for calcium were both 81%. The positive and negative predictive values at this level were 33% and 97%, respectively. Sensitivity and specificity for a threshold of 310 mg/24-hour urine for protein were 86% and 72%, respectively. The positive and negative predictive values at this level were 26% and 98%, respectively.

## Discussion

Preeclampsia is a pregnancy-specific, multisystem disorder characterized by the development of hypertension and proteinuria after 20 weeks' gestation. Renal excretion of calcium increases during normal pregnancy, and hypercalciuria in normal pregnancy is a consequence of an increased glomerular filtration rate [4,5]. Serum calcium levels in preeclampsia patients are similar to those in normotensives, but some studies have suggested that urinary calcium excretion is considerably reduced [6–9]. Taufield et al [1] noted marked hypocalciuria in patients with hypertensive disorders of pregnancy. Sanchez-Ramos et al [4] reported that excretion of calcium was reduced in the third trimester in women with preeclampsia compared with normotensive women. A study by Roelofsen et al [10] measured urinary calcium excretion in normal and complicated pregnancies, but failed to find hypocalciuria in preeclamptic women.

Compared with normal pregnancies, preeclamptic patients excrete significantly higher amounts of urinary protein. The increased albumin excretion in these patients appeared, on average, 9 weeks prior to the development of hypertension [11–15].

In our study, we found that low urinary calcium and higher urinary protein were risk factors for preeclampsia in asymptomatic pregnant women, when the tests were performed at 20–28 weeks' gestation. Seventy-six percent of our preeclamptic patients had hypocalciuria and 81% had proteinuria, defined by the respective cutoff points.

Measurement of 24-hour urinary calcium and protein excretion has advantages as a diagnostic test; it is noninvasive, inexpensive, and easy to carry out. The use of 24-hour urinary protein and calcium as early predictors will help to identify pregnant females at high risk of preeclampsia and prompt the initiation of education and prophylactic interventions (i.e. primary prevention, e.g. close prenatal care, calcium supplementation,

low-dose aspirin). These tests can also be used as selection criteria in research studies.

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