Diagnostic accuracy of urinary spot protein: creatinine ratio for proteinuria in hypertensive pregnant women - systematic review


CRD summary
This review found that the spot:creatinine ratio has reasonable accuracy for ruling out proteinuria of 0.3 g/day or more, but there are insufficient data on the accuracy of the spot albumin:creatinine ratio. These conclusions are supported by the results presented and are likely to be reliable.

Authors’ objectives
To determine the accuracy of the spot protein:creatinine ratio and the albumin:creatinine ratio for the diagnosis of significant proteinuria in hypertensive pregnant women.

Searching
MEDLINE and EMBASE were searched from 1980 to May 2007; the Cochrane Library was also searched. Keywords, which were reported, did not include a diagnostic filter. The reference lists of primary studies and guidelines for pregnancy hypertension were screened and experts in the area were contacted. Only studies written in English or French were included. Abstracts were excluded.

Study selection
Diagnostic accuracy studies that evaluated the urinary spot protein:creatinine ratio or the albumin:creatinine ratio, included urinary protein excretion over 24 hours as the reference standard, and were conducted in pregnant women of whom at least 80% had hypertension, were eligible for inclusion.

In most studies the spot protein:creatinine ratio was carried out before the 24-hour urine collection, but in some it was conducted after, before or after, or during the test. Most studies did not use the first urine sample of the day for the test. A variety of different laboratory methods were used to measure protein and creatinine, with various thresholds used to define a positive result. The women in the included studies had gestational hypertension, gestational hypertension with proteinuria of + or more (suspected pre-eclampsia), or any hypertensive disorder of pregnancy. The majority of studies only included women admitted to hospital; two excluded women who needed bed rest. Some studies excluded women with underlying medical disease such as pre-existing hypertension, diabetes, renal disease, urinary tract infection or bacteriuria. The outcomes reported in the review were the sensitivity, specificity, positive and negative likelihood ratios (LRs), and area under the curve (AUC).

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The studies were assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool, with studies being assigned a score based on the number of items fulfilled. The authors did not state how many reviewers performed the quality assessment.

Data extraction
Two reviewers independently extracted the data; any disagreements were resolved through consensus. Data on accuracy were extracted as the sensitivity, specificity, positive and negative LRs, method of agreement (e.g. Bland-Altman plots), receiver operating characteristic (ROC) curves, AUC and the proposed threshold for significant proteinuria. A conversion factor of 1.13 was used to transform results for the spot protein:creatinine ratio reported in mg protein/mg creatinine into SI units of mg/mmol. If positive and negative LRs were not reported, then these were calculated from the reported sensitivity and specificity. In addition, a threshold of 30 mg protein/mmol creatinine was selected and data reported in the articles were used to reconstruct 2x2 tables of test performance at this threshold. The sensitivity, specificity, and positive and negative LRs were calculated as close to this threshold as possible. Authors were contacted for missing information.
Methods of synthesis
Simple fixed-effect methods were used to pool the data on sensitivity and specificity at levels as close to the 30-mg threshold as possible. Pooled positive and negative LRs were estimated from pooled values of sensitivity and specificity. A sensitivity analysis was conducted by excluding studies that differed methodologically from all or most other studies. Threshold-related heterogeneity was assessed using the Littenberg-Moses regression method; pooling was only conducted in the absence of any evidence of such heterogeneity.

Results of the review
Thirteen studies (1,214 women) assessing the spot protein:creatinine ratio and two (225 women) assessing the spot albumin:creatinine ratio were included. Two studies only reported correlation coefficients and so were excluded from further analysis.

Study quality scores ranged from 7 to 12 out of a possible 14. The studies generally scored poorly on description of selection criteria, patient spectrum and definition of how the test was executed. Most of the studies were prospective and cross-sectional. Incomplete pairs of tests for analyses ranged from 11 to 32% of samples.

Spot protein:creatinine ratio: 9 studies (1,003 women) reported sufficient data to analyse a cut-point of 30 mg/mmol. There was no evidence of significant heterogeneity between the studies (p=0.94). The pooled sensitivity was 84% (95% confidence interval, CI: 78, 90), the pooled specificity 76% (95% CI: 73, 80), the pooled positive LR 3.53 (95% CI: 2.83, 4.49) and the pooled negative LR 0.21 (95% CI: 0.13, 0.31).

Spot albumin:creatinine ratio: 2 studies were identified. The sensitivity and specificity were 94% and 94% in one study that used a threshold of 2 mg/mmol, and 95% and 100%, respectively, in the second study that used a threshold of 27 mg/mmol.

Cost information
The authors stated that they were unable to find any formal economic evaluation of either of the tests in hypertensive disorders of pregnancy.

Authors' conclusions
The spot:creatinine ratio has reasonable accuracy for ruling out proteinuria of 0.3 g/day or more. There are insufficient data on the accuracy of the spot albumin:creatinine ratio.

CRD commentary
This review addressed a focused question that was supported by clearly defined inclusion criteria. The literature search was adequate and included some attempts to locate unpublished studies, thereby limiting the possibility of publication bias. The review was limited to studies published in English and French, and one study was excluded as it was not published in either of these languages; abstracts were also excluded. Appropriate steps were taken to minimise bias and error in the extraction of data, but is unclear whether such steps were also taken when assessing studies for inclusion and their quality. An appropriate quality assessment was conducted based on accepted criteria; however, a summary quality score was calculated which has shown to be inappropriate for these criteria. Some details of individual QUADAS items on which studies scored poorly were reported, but further details would have been preferable to the use of quality scores. The methods used to pool the sensitivity and specificity were adequate but may produce spurious results in some circumstances; the use of more sophisticated methods, such as the bivariate or hierarchical summary ROC methods, would have been preferable. Overall, the authors' conclusions are supported by the results presented and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that the spot protein:creatinine ratio is a reasonable test for ruling out proteinuria of 0.3 g/day or more. Data are too limited to advocate using the spot albumin:creatinine test in pregnant women.

Research: The authors stated the need for further data on the validity of the 30 mg/mmol threshold in relation to adverse pregnancy outcomes among women with suspected pre-eclampsia, the impact on test performance of the timing of these tests, the use of different protein and creatinine assays, and the accuracy of formulae for the estimation of
creatinine clearance in pregnancy with decreased use of the 24-hour urine collection. Given the apparent accuracy of the spot albumin:creatinine ratio, it would appear that this is also an area where further research is warranted, although the authors did not specifically discuss this.

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