Systematic review of accuracy of fetal urine analysis to predict poor postnatal renal function in cases of congenital urinary tract obstruction

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CRD summary
This well-conducted review found that none of the foetal urine tests investigated by the included studies showed sufficient accuracy to predict poor postnatal renal function. These conclusions are likely to be reliable.

Authors’ objectives
To determine the usefulness of foetal urine analysis in the prediction of poor postnatal renal function in foetuses with congenital urinary tract obstruction.

Searching
MEDLINE, EMBASE, CINAHL, the Cochrane Library, MEDION, SIGLE, Index to Scientific and Technical Proceedings, SciSearch, National Research Register and the Medical Conferences register were searched from inception to 2006; the search terms were reported. The bibliographies of primary studies and review articles were screened. No language restrictions were applied.

Study selection
Test accuracy studies of any foetal urine analysis test conducted in foetuses with ultrasound evidence of congenital urinary tract obstruction in which the reference standard consisted of any method to determine postnatal renal function or renal dysplasia in non survivors, and that provided sufficient data to construct 2x2 tables of test performance, were eligible for inclusion.

The specific tests investigated by the included studies were measurement of one or more of the following: cystatin C, beta2-microglobulin, sodium, potassium, chloride, calcium, IGF-1, IGFBP-3, osmolality, amino acids, creatinine, total protein, phosphorous, glucose, ammonia and urea. The studies used different thresholds to define an abnormal result and a variety of reference standards were used (full details were provided).

The included studies enrolled foetuses with prenatally suspected lower urinary tract obstruction, or ultrasound evidence of unilateral or bilateral obstructive uropathy/hydronephrosis, megacystis or bladder outlet obstruction. In some studies foetuses with chromosomal and/or structural anomalies, or female foetuses were excluded. Tests were performed between 12 and 36 weeks' gestation.

The outcomes reported in the review were the sensitivity, specificity and likelihood ratios (LRs).

Two reviewers screened studies for relevance and inclusion.

Assessment of study quality
The quality of the studies was assessed using the following items: prospective study design, consecutive patient enrolment, all index test results verified by the reference standard, and adequate description of the index test and reference standard.

One reviewer assessed study quality Any difficulties in quality assessment were resolved through input from a second reviewer.

Data extraction
The accuracy data were extracted as 2x2 tables of foetal urine result and postnatal renal function or outcome. The sensitivity, specificity and LRs, together with 95% confidence intervals (CIs), were calculated; 0.5 was added to all cells in all 2x2 tables.
One reviewer extracted the data onto a predesigned form. Any difficulties in data extraction were resolved through input from a second reviewer.

**Methods of synthesis**
The LRs were pooled using random-effects models if the studies had sufficient similar characteristics. Subgroup analysis was performed where there were at least 2 studies with similar characteristics; the subgroups were based on clinical criteria known to affect prognosis.

**Results of the review**
Twenty-three studies (572 pregnancies) providing 63 sets of 2x2 data were included; some studies provided data from more than one index test or reported data for different thresholds.

Study quality was generally poor: 6 studies enrolled consecutive patients, 8 studies were prospective, 20 studies reported >90% verification, 20 patients enrolled an appropriate patient spectrum, all studies reported blinding of tests, 4 studies provided an adequate description of the index test, and 4 studies provided an adequate description of the reference standard.

- **Sodium** (15 studies, 18 sets of 2x2 data): the sensitivity ranged from 29 to 100% and the specificity from 50 to 100%. Data were pooled for studies that used thresholds of >95th centile (3 studies), >100 milli equivalents (mEq)/L or 100 mmol/L (3 studies), or >100 mg/dL (3 studies). The pooled positive LR (LR+) ranged from 3.13 to 4.46 and the negative LR (LR-) from 0.37 to 0.44, suggesting poor accuracy for both ruling in and ruling out poor postnatal renal function.

- **Beta2-microglobulin** (11 studies, 17 sets of 2x2 data): the sensitivity ranged from 14 to 100% and the specificity from 23 to 100%. Data were pooled for studies that used thresholds of >2/2.5 mg/dL (4 studies), >10 mg/dL (2 studies), or >13 mg/dL (3 studies). The pooled LR+ ranged from 2.92 to 4.61 and the LR- from 0.46 to 0.53, suggesting poor accuracy for both ruling in and ruling out poor postnatal renal function.

- **Calcium** (9 studies, 11 sets of 2x2 data): the sensitivity ranged from 53 to 100% and the specificity from 27 to 100%. Data were pooled for studies that used thresholds of >95th centile (2 studies). The pooled LR + at this threshold was 6.65 (95% CI: 0.23, 190.96), suggesting some ability to rule in poor postnatal renal function, but the CI was very large. The pooled LR- was 0.19 (95% CI: 0.05, 0.74), suggesting that this threshold also showed some ability to rule out poor postnatal renal function. At a threshold of >0.95 or 1.25 mmol/L (3 studies), the pooled LR+ was 3.44 and the LR- 0.43, suggesting poor accuracy for both ruling in and ruling out poor postnatal renal function.

- **Chloride** (6 studies, 7 sets of 2x2 data): both the sensitivity and specificity ranged from 50 to 100%. Data were pooled for the studies that used a threshold of >90 mmol/L or >90 mEq/L (3 studies): the pooled LR+ was 3.09 and LR- 0.46, suggesting poor accuracy for both ruling in and ruling out poor postnatal renal function.

- **Osmolality** (4 studies, 5 sets of 2x2 data): both the sensitivity and specificity ranged from 50 to 100%. All studies reported data for similar thresholds (>200 or 210 mOsm/L), so the data were pooled: the pooled LR+ was 3.41 and the LR- 0.33, suggesting poor accuracy for both ruling in and ruling out poor postnatal renal function.

- **Total protein** (3 studies, 4 sets of 2x2 data): the sensitivity ranged from 50 to 88% and the specificity from 71 to 91%.

Other single and combined analytes were only evaluated in single studies; full results were presented in the paper.

**Authors’ conclusions**
None of the tests investigated showed sufficient accuracy to predict poor postnatal renal function.

**CRD commentary**
This was generally a well-conducted and clearly reported review. The objective was focused and the inclusion criteria were clearly defined. The literature search was extensive and included attempts to locate unpublished studies. Details on the review process were reported and included appropriate steps to minimise bias and errors in the selection of
studies, although such steps were not taken in the extraction of data or quality assessment. The quality assessment used appropriate criteria and the results were clearly summarised in a figure. The analysis was complex because of the large variety of measurements reported by the studies, different thresholds used and differing reference standards. However, appropriate data were clearly presented and data were only pooled for studies that were sufficiently similar. Heterogeneity appears to have been assessed statistically, but the results of this assessment were not reported. 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 none of the analytes investigated have sufficient accuracy to be clinically useful.

Research: The authors did not state any implications for further research.

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