Is the albumin:creatinine ratio the best screening tool for proteinuria?

Dr Thomas J. Cade
Consultant Obstetrician
Royal Women’s Hospital, Melbourne

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Overview

1. Preeclampsia summary (brief)
2. Is proteinuria still relevant?
3. Preeclampsia v PIH – is prompt differentiation important?
4. Traditional testing and quantification
5. Why spot specimens perform at least as well as a 24-hour collection
6. What is the utility of the spot albumin:creatinine ratio compared to the protein:creatinine ratio
Pre-eclampsia summary

- Highly important cause of morbidity and mortality in Western and developing world
- 2nd in direct maternal deaths in UK and 3rd in Australia
- Increasing prevalence (worldwide 4.6%):
  - Older population
  - Increasingly sophisticated reproductive medicine
  - Increasing obesity and diabetes
Pre-eclampsia definitions

• MUST have hypertension (proteinuria by itself does not count)
• Must be SBP $\geq 140$ and/or DBP $\geq 90$ on several occasions over a period of time
• Must have one additional feature (long list)
• Proteinuria is not mandatory anymore (SOMANZ and ISSHP) but most common additional feature
• Oedema is not sensitive nor specific but new rapid onset may prompt investigation
THE SOMANZ GUIDELINE FOR THE MANAGEMENT OF HYPERTENSIVE DISORDERS OF PREGNANCY

2014

Contents lists available at ScienceDirect

Pregnancy Hypertension: An International Journal of Women’s Cardiovascular Health

journal homepage: www.elsevier.com/locate/preghy

The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP

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2210-7789/© 2014 Published by Elsevier B.V. on behalf of International Society for the Study of Hypertension in Pregnancy.
So... does proteinuria matter?

- Recent very high quality data suggesting level of proteinuria is related to poor outcome
- This may not apply to rapidly progressive proteinuria
- Should proteinuria be part of the definition for severity?
- It IS the most common additional feature to hypertension therefore the best diagnostic discriminant
- Most likely to assist in early detection

Is prompt diagnosis important?

- Western countries have relatively low morbidity and mortality rates because of this
- Accurate planning of gestation for delivery
- Instigation of more frequent monitoring
- Admission vs outpatient planning
- Future treatment (current strategies are more focussed on prevention)
  - Sulfasalazine
  - Pravastatin
  - Esomeprazole
Preeclampsia v PIH

- Proteinuria most common diagnostic feature therefore best discriminant between pre-eclampsia and PIH
- Are these treated differently these days?
- Possibly depends if you believe the HYPITAT trials
- Current NICE guidelines for preeclampsia
  - Definitely deliver from 36 weeks
  - “Offer to women with mild-moderate..” between 34 and 36 weeks
- WHO leans more toward expectant management until 37 weeks
Preeclampsia v PIH

- Hypitat II: PIH or “non-severe PET” between 34 and 37 weeks to expectant v immediate IOL
- 1/3 expectant group delivered < 37 weeks
- Immediate IOL: incr risks of prematurity but trend to decr maternal morbidity.
- IF you believe Hypitat I and II, then you may trend to later deliveries for mild pre-eclampsia and earlier deliveries for PIH
- Thus: is differentiating the two really important?
- If no: is an accurate proteinuria screening test really important?
Traditional Proteinuria Testing
The 24-hour collection

- Supposedly the gold standard but:
- Data suggest up to 25% variation in samples collected from the same patient\(^1\)
- Compared to a spot sample
  - More time consuming
  - Slower diagnosis
  - Patients do not like
  - More admissions

The Spot Protein:Creatinine Ratio (PCR)

- Much more convenient but is it accurate?
- 1997 Australian study one of the earliest\(^1\)
  - 30 mg/mmol best discriminatory value
- Subsequent studies differing results
- Further 2011 Australian study of patients in single centre using a discriminatory value of 30 mg/mmol confirmed utility.
- Most reputable guidelines include it now:
  - SOMANZ: “24-hour collection rarely required”

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The Spot Albumin:Creatinine Ratio (ACR)

- Primary test of choice for many physicians
- Shown to be superior in diabetics for predicting adverse outcome
- Extremely heterogenous data in pregnancy
- Semi-quantitative dipstick, automated analyser, laboratory
- Best study: 27 mg/mmol corresponds well to 300 mg/day
- No study compared ACR to PCR directly

The Spot Albumin:Creatinine Ratio (ACR)

- We aimed to compare tests
- Prospective, paired specimens on 1st void of day
- Two outcomes:
  - Same value for known cut-off of 30 mg/mmol proteinuria
  - If either is more predictive of adverse pregnancy outcome
- Also interested in continuing to examine if the level of proteinuria (on either test) is a poor prognostic sign
The Spot Albumin:Creatinine Ratio (ACR)

- 18 months, 254 tests in 181 patients
- Highly correlated (no surprise)
The Spot Albumin:Creatinine Ratio (ACR)

- PCR = 13.75 + 1.22\times ACR
- Therefore:
  - 30 mg/mmol PCR = 13.4 mg/mmol ACR
- Area under ROC curve 0.98
The Spot Albumin:Creatinine Ratio (ACR)

- For 100% specificity and sensitivity:
  - ACR < 2.3 mg/mmol definitely not proteinuric and ACR > 17.2mg/mmol definitely is
- However given the close correlation,
  - 13.4 mg/mmol is reasonable (much less than the previously suggested 27)
- Neither better at predicting adverse outcome
- Level of proteinuria (on either test) not related to adverse outcome
Future Research

• Where is the extra protein coming from (13.4 mg/mmol ACR v 30 mg/mmol PCR)
  » Product of laboratory methods?
  » Non albumin proteins - ?heavier than albumin but small contribution by volume
  » Non-immune albuminuria

• Inter-lab variations (ACR is much more reproducible)

• Examine using a policy of 13.4 mg/mmol ACR vs 30 mg/mmol PCR - ?RCT
Summary

- Proteinuria is important in diagnosing pre-eclampsia but probably not in predicting severity.
- Implications for frequency of monitoring, potential for other complications and timing of delivery (and future novel agents).
- PIH and PET are not created equal recent evidence.
- 30 mg/mmol on PCR is accepted by all reputable guidelines.
- Unclear role for ACR – if used 13.4 mg/mmol is a reasonable cut-off.