Mini-Review

Laboratory Reporting of Urine Protein and Albumin

Graham RD Jones[1,2]
[1]Department of Chemical Pathology, SydPath, St Vincent's Hospital, Sydney, Victoria St, Darlinghurst, NSW 2010, Australia.
[2]Faculty of Medicine, University of NSW, Sydney, NSW 2052, Australia.
For correspondence: Dr Graham Jones, gjones@stvincents.com.au

Abstract
Communication between pathology laboratories and clients involves more than just a result. There may be advice on recommended specimen type as well as the units and reference intervals used to report results. Between-laboratory variability in these factors has the potential to cause unnecessary confusion and even to lead to variation in interpretation for samples sent to different laboratories. A survey of Australian and New Zealand laboratories covering sample recommendations, specimens received, units and reference intervals for urine albumin and urine protein was conducted through the Royal College of Pathologists of Australasia Quality Assurance Program (RCPA QAP). The results confirm earlier findings of wide between-laboratory variability in all these factors. It is proposed that only recommendations developed by relevant professional societies and adopted by all laboratories can lead to reduction in this variability.

Introduction
Pathology is information. The purpose of pathology testing is to generate new information about a patient and communicate that information so that decisions can be made to improve the health of the patient. Correctly, laboratories apply considerable effort to ensure the quality of the testing processes which generate the new information. By contrast, the factors involved in communicating that information are sometimes less well considered. Some of the factors which must be considered when communicating with doctors about tests are shown in Table 1. This paper addresses some of these issues in communicating collection recommendations and results for tests of urine protein and albumin.

We need to consider with whom we are communicating. There are approximately 60,000 medical practitioners in Australia. Although these doctors are all registered to practice medicine, they represent a wide range of ages, medical schools, post-graduate training, mother tongues and clinical experience. Our results are also often reviewed by allied health personnel such as nurses, dietitians, diabetes educators, pharmacists and others. The variation in educational background is even wider for these recipients of our reports, especially with regard to the field of laboratory medicine. Results are now often viewed by patients themselves. There are, of course, over 20 million potential patients in Australia, and the background of these laboratory customers is vastly more variable again. The challenge to provide a clear transfer of our information to all possible recipients is not a trivial issue, however. It is a significant component of our professional responsibility. As a start, uniformity of information from different laboratories should facilitate the communication process.

There are many formats which are used to communicate pathology results. These include paper reports, telephone calls, computer screens and other e-messaging systems. Within these broad categories there are many subvariations with different report formats and data subsets. We need to provide results which are clear, unambiguous and complete in whichever medium they are transmitted. There is also information we transmit concerning recommendations for testing, covering such items as patient preparation, specimen collection and handling. Again this material may be presented in many different forms and needs to be suitable for patients as well as doctors.

An additional factor guiding our choices in the field of results reporting comes with the development of databases in doctors' desktop software and locations which can accept results in 'atomised' format (i.e. as discrete data points, for example with the use of HL7 messaging). The results from different laboratories may then be combined in the program for auditing, graphing or other purposes. The requests for this functionality are frequently related to diabetes testing

Table 1. Variables in reporting test results and supporting information.

Information to Support Specimen Collection
Indications for test requesting
Patient preparation
Specimen type/tube type
Specimen handling
Variables in Test Reporting
Test name
Units
Significant figures of result
Reference intervals/decision points
Interpretative comments
Formula (for calculated tests)
Inclusion of inputs (for calculated tests)
Specimen received (timed, spot, time of day)

and specifically relevant to urine albumin measurements. Variability in the reporting factors described above may limit the ability to successfully combine result in these settings.

In order to address the current variability in reporting issues with urine albumin and protein, in late 2009 a survey was conducted among laboratories in Australia and New Zealand through the RCPA QAP. The total number of laboratories to which survey forms were distributed was approximately 120. The survey attracted 52 responses with a breakdown as follows: 44 Australia, 8 New Zealand; 37 public, 15 private; 39 main laboratory, 10 branch laboratory; 10 with fewer than 100 patient episodes per day, 25 with between 100 and 1000, and 10 with over 1000 patient episodes per day. (Note that for this and other sections of the survey, the numbers may not add up to the expected numbers as responses were not received from all respondents for all questions). The survey represents the users of all major analytical systems with Roche Hitachi/Cobas, Roche Integra, Siemens Dimension, Abbott Architect and Olympus analysers each represented by five or more respondents. The Beckman-Coulter Immage, Ortho Clinical Diagnostics Vitros, Siemens Vista and Siemens Prospec were each represented by fewer than five responses.

The results of the survey for urine albumin and urine protein are shown in Tables 2 and 3 respectively for all participating laboratories in Australia and New Zealand, with the New Zealand responses separated out in parentheses. They are discussed further below.

Sample Type Recommendations and Samples Received

For laboratories where advice was offered on the preferred specimen type for measurement of urine albumin, there was a wide disparity in recommendations covering 24 h samples, other timed samples, random spot samples and first morning spot samples. There were, however, significantly more laboratories receiving random spot samples than suggested by their recommendations. The situation for urine protein was similar to urine albumin. However, the sample type was markedly in favour of 24 h samples or random spot samples at the expense of other timed samples or first morning samples. The low numbers of first morning samples received may indicate a lack of coding for the sample time in the computer systems and these samples being included with the random samples.

Reporting Units

Urine albumin concentration was far more commonly reported in mg/L (n=38) than in g/L (1). However, there was a lack of uniformity for timed samples with μg/min (20) more common than mg/day (12) or g/day (2). For the albumin/creatinine ratio, mg/mmol (21) and its numerical equivalent of g/mol (5) were the units used.

By contrast, urine protein was more commonly reported in g/L (24) than mg/L (10), and g/day (32) than mg/day (9). For the protein/creatinine ratio, mg/mmol (12) was most common followed by the numerically equivalent g/mol (8) with mg/mg (1) and g/mol x 100 (1) being rarely used.

In seeking uniformity of reporting for urine protein, the decision is between mg/L (and per day) in line with urine albumin reporting, or g/L (and per day) which would better reflect current practice.

Reference Intervals

With regard to reference intervals, a very wide variation was evident in the responses. For samples where a reference interval was given for albumin concentration, the upper limit of the interval ranged from 15 to 35 mg/L, the albumin excretion rate from 15 to 34 μg/min, and the albumin/creatinine ratio from 1.0 to 3.5 mg/mmol, a 3.5-fold variation.

It is of note that even where decision points have been recommended, they are seldom brought into practice. For example, the decision points for microalbuminuria of 2.5 (male) and 3.5 (female) mg/mmol that have been recommended in Royal Australian College of General Practitioners (RACGP) guidelines since at least 2005[1] are in use in only a minority of laboratories. It would seem that promotion of a guideline to all relevant parties may be as important as developing it in the first place.

Table 2. Urine albumin sampling and reporting – current practice in Australasia (results of RCPA QAP survey conducted in 2009 – total results with NZ numbers in brackets*).

Urine albumin – sample type recommended by laboratory

Sample	24 hour	Other timed sample	Random spot sample	First morning spot sample
Total (NZ)	18 (0)	18 (1)	26 (7)	16 (0)

Urine albumin – received sample type
(number of laboratories receiving half or more of their samples of the type shown)

Sample	24 hour	Other timed sample	Random spot sample	First morning spot sample
Total (NZ)	5 (0)	7 (0)	35 (7)	11 (1)

Urine albumin – spot urine samples – reporting units

Quantity	Concentration			Albumin/creatinine ratio	
Units	mg/L	g/L	µg/mL	mg/mmol	g/mol
Total (NZ)	38 (6)	1 (0)	1 (0)	21 (1)	5 (1)

Urine albumin – timed urine samples – reporting units

Quantity	Concentration		Excretion rate		
Units	mg/L	g/L	mg/day	g/min	g/day
Total (NZ)	33 (5)	1 (0)	12 (2)	20 (1)	2 (0)

Timed urine albumin concentration upper reference limit (mg/L)**

Limit	15	18	20	25	30	25 (1st)/ 35 random
Total (NZ)	1 (1)	1 (0)	11 (0)	1 (0)	8 (4)	1 (0)

Timed urine albumin excretion upper reference limit (µg/min)**

Limit	15	20	30	34
Total (NZ)	4 (0)	20 (0)	1 (0)	2 (1)

Urine albumin/creatinine ratio upper reference limit (mg/mmol)**

Limit	1.0	2.0	2.5	2.5/3.0#	2.5/3.5#	3.0	3.5
Total (NZ)	3 (0)	2 (0)	5 (1)	1 (0)	7 (0)	1 (0)	10 (3)

* Numbers may not add to the total due to missing data, the format not being used by a laboratory, or multiple answers possible.** For reference intervals, the upper limits shown (X) represent limits expressed as both '<X' and '0-X' or very similar values and thus all may not indicate exactly the same decision point. # Male limit/female limit.

Table 3. Urine protein sampling and reporting – current practice in Australasia (results of RCPA QAP survey conducted in 2009 – total results with NZ numbers in brackets*).

Urine protein – sample type recommended by laboratory

Sample	24 hour	Other timed sample	Random spot sample	First morning spot sample
Total (NZ)	29 (4)	1 (0)	11 (3)	1 (0)

Urine protein – received sample type
(number of laboratories receiving half or more of their samples of the type shown)

Sample	24 hour	Other timed sample	Random spot sample	First morning spot sample
Total (NZ)	29 (4)	1 (0)	29 (3)	12 (0)

Urine protein – spot urine samples – reporting units

Quantity	Concentration		Protein/creatinine ratio				
Units	mg/L	g/L	mg/mmol	g/mmol	100 x g/mmol	g/mol	mg/mg
Total (NZ)	10 (1)	24 (3)	12 (0)	2 (0)	1 (0)	8 (1)	1 (0)

Urine protein – timed urine samples – reporting units

Quantity	Concentration		Excretion rate	
Units	mg/L	g/L	mg/day	g/day
Total (NZ)	9 (1)	16 (2)	9 (0)	32 (6)

Timed urine protein concentration upper reference limit (g/L)**

Limit	0.10	0.12	0.15	0.18
Total (NZ)	7 (1)	3 (0)	6 (1)	1 (0)

Timed urine protein excretion upper reference limit (g/day)**

Limit	0.10	0.15	0.22	0.30
Total (NZ)	1 (1)	32 (5)	5 (0)	1 (0)

Urine protein/creatinine ratio upper reference limit (mg/mmol)**

Limit	10	13	15	23	30	35
Total (NZ)	3 (0)	3 (0)	2 (0)	4 (0)	4 (0)	1 (0)

* Numbers may not add to the total due to missing data, the format not being used by a laboratory, or multiple answers possible. ** For reference intervals, the upper limits shown (X) represent limits expressed as both '<X' and '0-X' or very similar values and thus all may not indicate exactly the same decision point.

The differences in reference intervals may be expected to indicate differences in assay performance or in the populations being tested. An examination of the RCPA QAP data showed that for urine albumin, with the exception of the Siemens Dimension method, the difference between commonly used methods is within approximately +/-10% rather than the factor of two or three seen in the reference intervals. Given that the typical assay CV is about 10%, most laboratories would be expected to easily identify and respond to a shift of 30% within their laboratory. Thus the post-analytical issue of the reference intervals is contributing more to variation in patient classification than any other laboratory action.

Respondents were asked for the source of their reference intervals, with 5 using local data, 14 using those determined at a central laboratory, 15 using manufacturer recommendations, 19 deriving them from the literature and 4 indicating that they were unsure of the source. Thus laboratories had been active in finding data on which to base the intervals. My belief is that this is the likely outcome of the laboratory-based governance environment in which we operate. Even if each laboratory were provided with the same information, I suspect that we would all interpret it differently and reach a range of different conclusions. When we are able to select the data we will use and the principles on which the interval or decision points will be based, the variation becomes even wider. I believe that to facilitate the delivery of the same information to clients from different laboratories, national guidelines on these matters are obligatory.

For both albumin/creatinine ratio and protein/creatinine ratio there are also the analytical and reporting requirements for urine creatinine measurement. The diversity of urine creatinine reference intervals was considerable, with 27 different sets of reference intervals in use: 18 intervals were used by 23 laboratories with the same interval for males and females. Nine different intervals were used by laboratories with partitioning for sex. The lower reference limit varied between 5 and 10 mmol/L and the upper limit between 12.5 and 25 mmol/L indicating a two-fold difference between laboratories for reference intervals. Again, these differences are wider than seen in the RCPA QAP program for urine creatinine.

Conclusions

From the data presented here, it is clear that the information being transmitted by Australasian laboratories to clients is needlessly confusing and potentially confounding. An example is in the use of different units for the same measurements. These unnecessary differences may obscure the message we are aiming to transmit. Similarly, the promotion of different sample types contributes to practice variation which makes comparison of results from different locations more complex. The different reference intervals in use may have the greatest effect, leading to fundamentally different information from a test (i.e. 'normal' vs 'abnormal') depending on the laboratory performing the test. A similar wide variability in preferred samples and units for urine albumin has been described for many European countries where the authors also support standardisation of practice.[2]

A very similar survey was conducted using the same methodology in late 2005 and the results are not significantly different to those presented here.[3,4] Thus in the absence of external recommendations, there has been no significant consolidation of sample type, units or reference intervals over the last four years. In both surveys there is generally less variability amongst the New Zealand laboratories than in the total group, but significant variability remains.

At the time of writing there is a working party of the RCPA, Australasian Association of Clinical Biochemists, Kidney Health Australia, Australian and New Zealand Society of Nephrology, Australian Diabetes Society and RACGP aiming to address some of the issues raised in this paper. I believe this type of approach is required in many fields of laboratory medicine to deliver a clear and consistent message to the many users of our services.

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References

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