Singapore Journal of Obstetrics and Gynaecology
2009; 40(1): 27-33

Comparison of Overnight, Day and Single Void Samples with 24 Hour Urine Collection in the Assessment of Preeclamptic Albuminuria

Neena Chuni

ABSTRACT

Objective : To evaluate whether shorter collection periods of urine could substitute the gold standard of 24-hour collection for preeclamptic albuminuria.

Methods : A prospective study on 42 preeclamptic women with a urine test strip value of 2+ was carried out at the Manipal College of Medical Sciences in Nepal over two years. For each woman three timed single void samples and two 12-hour (day and night) samples were collected and the albumin concentration in each of these samples were compared with the 24-hour urinary albumin excretion determined after adding these samples to account for 24-hour urine collection.

Results : The 12 hour night collection of urine matched most closely with the 24-hour urine collection (median difference 30mg/L, interquartile range - 198 to 220mg/L); followed by the 12-hour day collection (median difference -55.5mg/L, interquartile range - 264 to 116mg/L). The albumin concentration in single void samples correlated poorly with the 24-hour collection; however , the single void sample taken at beginning of the collection was closest to the 24-hour gold standard (median difference - 97mg/L, interquartile range -1108 to 426mg/L).

Conclusion : 12-hour night samples can be used to replace the 24-hour gold standard urine collection for preeclamptic proteinuria, being equally accurate, easier and quicker to collect. Single void samples were inaccurate and are not recommended for assessing urine albumin excretion in preeclamptic women.

Key words: Preeclampsia, 24-hour urine sample, albuminuria, single void urine sample, 12-hour urine sample.

Dr Neena Chuni, MS, FICOG,
Senior Consultant Obstetrics & Gynaecology,
Indira Gandhi Memorial Hospital,
MALE 20402, Republic of Maldives.

Manipal College of Medical Sciences,
Department of Obstetrics & Gynaecology,
POKHARA 33701, Nepal.

Correspondence to:
Dr Neena Chuni,
#301, Purva Iris,
54, MSO Colony, Cox Town,
BANGALORE 560 005, India.
Emai : nchuni@gmail.com
In Maldives : +960-3303539
In India : +91-80-41253224
Mobile : +960-7571865
Fax No : +91-80-41253224

INTRODUCTION

Hypertensive disorders complicate 7% of pregnancies and contribute to 12% of all maternal deaths worldwide [1]. Patients with significant proteinuria have a significant reduction in the mean birth weight for gestational age compared to patients with hypertension alone, due to intrauterine growth restriction. In contrast, in women with hypertension alone, the mean birth weight for gestational age is the same as that in normotensive women [2]. Therefore, early detection and timely management of patients with proteinuria is beneficial to both the mother and the fetus [2,3,4,5,6].

Screening for albuminuria is a part of standard antenatal care, performed by urine dipstick analysis on a random spot urine sample. If urine dipstick for albuminuria shows a result of 2+ or more in absence of bacteriuria, the gold standard of 24-hour collection for quantification of albumin is carried out. However, 24-hour collections are cumbersome, difficult to perform on outpatients and may also be inaccurate if collections are incomplete. In most situations where management decisions have to be taken quickly, results of 24-hour collections may not keep pace with rapidly worsening clinical situations. In such situations dipstick method has to be relied on, but this method is fraught with error and correlates poorly with 24-hour urinary protein [7,8]. The accuracy of shorter collection periods needs to be correlated with the gold standard of 24-hour collections. In pregnant women, particularly if admitted in hospital, the circadian variation in albumin excretion is smaller or absent [9]; therefore, it may be possible to use shorter collection periods.

The aim of this study was to evaluate the accuracy of shorter collection periods of urinary albumin excretion as a substitute for the 24-hour gold standard.

METHODS

Forty two women with pre-eclampsia admitted to the antenatal ward, in the Department of Obstetrics and Gynaecology at Manipal College of Medical Sciences, Pokhara, Nepal, between June 2007 and May 2008 were included in the study. Inclusion criteria were proteinuria of at least 2+, equivalent to an albumin concentration of 500mg/L or greater, performed by urinary dipstick method. Exclusion criteria included women with history of urinary tract infection and fever, confirmed by urine culture examination of midstream urine; and women with pathological vaginal discharge. Women with preexisting chronic hypertension and other coexisting medical disorders like anaemia, hypoproteinemia, liver disease, renal disease and diabetes mellitus were also excluded from the study.

There were 30 nulliparous and 12 multiparous women. All women were booked antenatal cases and had been attending outpatient antenatal clinic since pregnancy was diagnosed in the first trimester. Hence baseline weight and blood pressure values of all patients since the first trimester were recorded. No dietary alterations were recommended but all patients were on moderate bed rest of at least 7 to 8 hours during day time. Thirty six patients were on antihypertensive drugs, mainly alphamethyldopa and nifedipine. None of the women were smokers. Informed consent was obtained from all women.

All of these patients were scheduled for a 24-hour urine collection on the basis of proteinuria greater than or equal to 2+ by dipstick method. In addition, three single void urine samples were obtained and two 12-hour samples (day and night) were collected. All samples were collected over a period of 24 hours and collection started on the morning following admission to the hospital. The women were instructed on the method of collection and were given clearly labelled containers. Each container was marked with the patient's name, number of the container and collection time. A 12-hour day sample was obtained from 0700 hours to 1900 hours and 12-hour night sample from 1900 hours to 0700 hours. Single void values were obtained from 3 samples by first voiding at the beginning of collection at 0700 hours, again at 1900 hours and finally at 0700 hours at the end of collection. All the samples were mixed to form a 24-hour sample. The urine samples were stored at 4°C before analysis. The Beckman Array protein system which uses the rate nephelometry method for analyzing urine albumin was used. All tests were analysed by well trained technicians at the laboratory services of the Institution.

Since the albumin levels in spot urine samples were reported in milligrams per litre, all values were presented in the same units. The comparisons between 24-hour collection and the other samples were depicted graphically. Median differences between the 24-hour sample and other samples were calculated along with the interquartile ranges. All data were entered into the computer and analysed using SPSS software.

RESULTS

There were 38 complete collections; for 4 women either one or both the single void spot samples were missing (Table1). The mean age of the patients was 25 years and mean gestational age at the time of admission was 236 days. Mean weight gain of the

patients during pregnancy was 14.6 kg. The mean systolic and diastolic blood pressure of the patients during early pregnancy were 116mm Hg and 76mm Hg respectively, whereas these values at the time of admission were 156mm Hg and 103mm Hg. The mean 24 hour urine collection was 1.9 L (Table 2). The mean plasma albumin concentration was 34.7g/L (SD 3.5g/L) (reference interval : 29-43g/L); mean plasma uric acid concentration was 3.9mg/dL (SD 0.34mg/dL) (reference interval: 3.1-4.5mg/dL) and the mean serum creatinine level was 0.95mg/dL (SD 0.22mg/dL) (reference interval: 0.6-1.4mg/dL).

The median difference between the 24-hour and day 12-hour collection was -55.5mg/L (interquartile range - 264 to 116mg/L) whereas median difference between 24-hour collection and night 12-hour sample was 30mg/L (interquartile range - 198 to 220mg/L); thus, the night sample correlated better with the 24-hour sample.

The median difference in albumin concentration between the 24-hour and first spot sample was 97mg/L (interquartile range - 1108 to 426mg/L). The median differences between the 24-hour albumin concentration and the second and third single void samples were 334mg/L (interquartile range - 798 to 80mg/L) and 449mg/L (interquartile range - 720 to 190mg/L) respectively; thus the first sample taken in the morning at the beginning of the collection correlated best.

The relation between urine albumin concentration in the single void, 12-hour (day and night) and 24-hour collections are depicted graphically in Figure 1. Albumin concentrations in the day and night samples correlate well with the 24-hour sample as there is less dispersion (Figure 1a,b); the night sample correlated best. The albumin concentrations in the 3 single void samples correlated poorly with the albumin concentration in the 24-hour sample (Figure 1c,d,e) as there is more graphical dispersion. The albumin excretion was overestimated in all samples, except the night sample and the first void sample, as indicated by the negative values for median differences. Difference in albumin concentrations between the 24-hour sample and the 12-hour night sample has the least variability and correlates best with the 24-hour collection.

DISCUSSION

In this study, urine albumin concentration measured in the samples collected over 12- hours showed good correlation with the 24-hour urinary albumin concentration, whereas the single void specimens showed very poor agreement with the 24-hour collection. Therefore, single void specimens are not recommended as a substitute for the gold standard of 24-hour collections. Overestimation of albumin excretion may lead to planned interventions such as preterm delivery whereas underestimation may lead to delay in interventions and increased maternal and perinatal morbidity.

In rapidly deteriorating clinical situations where management decisions have to be taken quickly, frequent urine analysis are required which should be accurate, easy to perform and inexpensive. A 24-hour collection is tedious to perform and takes at least 25 hours, thus delaying management decisions. Often, decisions are based on single void specimens which are inaccurate. Dipstick urine protein is inaccurate for diagnosis of pre-eclampsia because 64-66 percent of the patients who had negative or traces of protein still had significant proteinuria [5,10]. Single void urinary albumin/creatinine ratio has been advocated as a valid estimate of 24-hour urine protein [11-14], whereas other studies have reported a poor correlation of this value [15,16].

Some studies have reported a diurnal variation in urinary albumin excretion especially in diabetic patients [17]. Protein excretion tends to increase with ambulation and upright body position, which produces renal vasoconstriction and altered permeability of the glomerular barrier [18]. These physiological factors are thought to produce a diurnal variation in protein excretion. This study was performed on women who were on a regimen of bed rest, therefore variability in protein excretion on account of posture is unlikely. In this study, both the 12-hour samples correlate well with the 24-hour sample, hence it is unlikely that this variability influences results in patients with pre-eclampsia. Even in an outpatient setting, patients with pre-eclampsia are usually prescribed a regimen of bed rest, and a 12-hour collection would be easiest to complete. A 12-hour collection, particularly the night sample is recommended as it correlates best with the gold standard, is easy to collect and gives results quickly in rapidly changing clinical situations.

Table 1. Urine albumin Excretion in mg/L in different samples

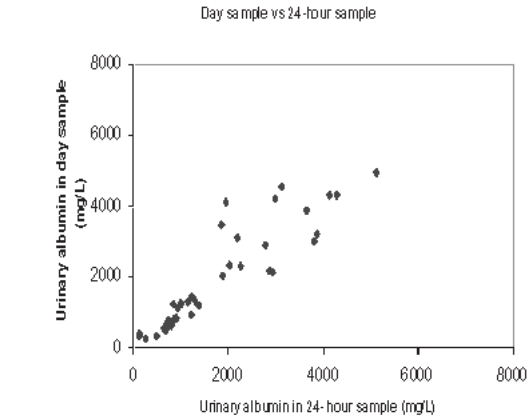
Participant	24 hour sample	Day sample	Night sample	First spot sample	Second spot sample	Third spot sample
1	116	323	84	288	386	260
2	4121	4342	2962	3880	7420	5480
3	723	768	812	1540	1022	1320
4	676	536	648	516	476	2310
5	4282	4316	3612	5188	4248	7210
6	2172	3114	2450	1570	2770	2430
7	732	762	794	1452	602	1450
8	902	844	1168	2410	1360	1421
9	1208	1431	1406	5120	2670	3210
10	1942	4113	1366	3120	5840	502
11	2240	2320	2140	520	678	876
12	1365	1224	1872	5210	1370	2118
13	816	1260	873	1924	1526	1510
14	778	742	856	1460	701	1140
15	5124	4952	5721	4132	5690	5560
16	682	581	956	544	920	1210
17	788	656	922	541	898	760
18	246	262	278	214	940	280
19	2010	2346	1656	3120	2420	2730
20	1274	1340	1284	1180	1480	1940
21	920	1128	854	2610	1456	1570
22	1866	2040	1722	1440	4232	1760
23	1213	940	1360	2700	720	2290
24	1240	1417	1020	356	2780	640
25	640	580	678	1150	720	1040
26	840	800	642	698	1450	650
27	980	1260	940	848	4110	592
28	2780	2920	2420	2170	3120	1850
29	2980	4230	3840	4220	4530	3450
30	2850	2190	2640	2270	3950	1250
31	3112	4570	1708	2760		4230
32	3640	3890	3250	3540	4170	6120
33	1140	1310	1020			3100
34	3860	3210	4450		4120	5780
35	482	356	712	356	740	880
36	1850	3492	1480	2980	5760	476
37	658	520	890	1360	876	1120
38	995	1268	920		3410	770
39	2918	2136	2566	2642	3716	1230
40	3794	3010	3210	2680	3450	1850
41	118	398	76	296	394	256
42	728	716	976	2100	1056	1276

Table 2. Patient characteristics

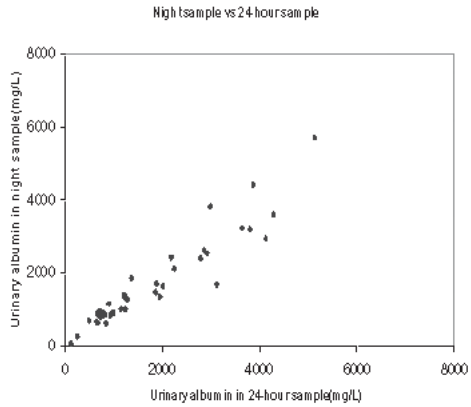
	Mean	Meridian	Range
Age of patient (years)	25	24	18-38
Gestational age at admission (days)	236	239	207-261
Weight gain during pregnancy (kg)	14.6	14.8	12.1-16.8
Systolic BP early pregnancy (mmHg)	116	117	100-130
Diastolic BP early pregnancy (mmHg)	76	76	68-86
Systolic BP at admission (mmHg)	156	159	114-180
Diastolic BP at admission (mmHg)	103	100	90-120
24-hour urine collection (g/L)	1.7	1.2	0.12-5.1
24-hour urine collection (L)	1.9	1.9	1.1-2.5

Table 1a to e. Relation between albumin concentration in 12 hour day, night and first, second and third single void specimens

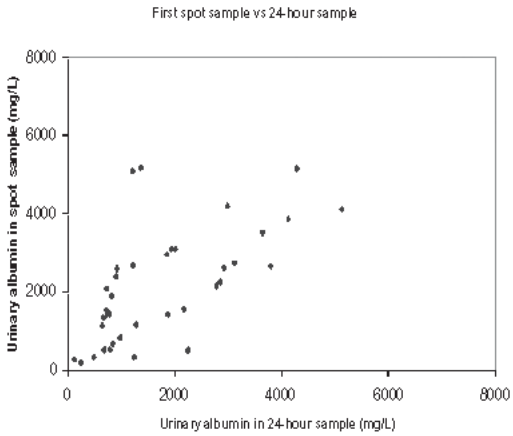
1-a



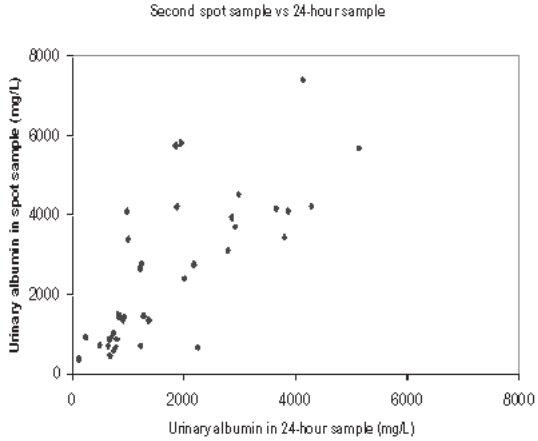
1- b



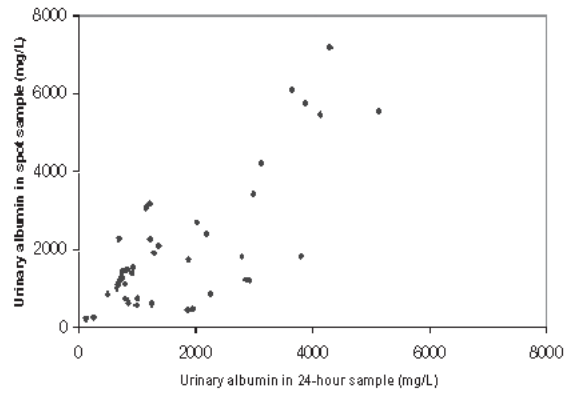
1 – c



1 - d



1 - e



REFERENCES

1. *World Health Organisation: Reduction of Maternal Mortality: A Joint WHO/UNFPA/UNICEF/WORLD BANK STATEMENT,1990.*

2. *Macgillivray I. Is mild pre-eclampsia harmful to the baby? Isr J Med Sci 1977;12: 500-3.*

3. *Waugh JJ, Clark TJ, Divakaran TG, Khan KS, Kilby MD. Accuracy of urinalysis dipstick techniques in predicting significant proteinuria in pregnancy. Obstet Gynecol 2004; 103(4):769-77.*

4. *Waugh JJ, Bell SC, Kilby MD, Blackwell CN, Seed P, Shennan AH, et al. Optimal bedside urinalysis for detection of proteinuria in hypertensive pregnancy: a study of diagnostic accuracy. Br J Obstet Gynaecol 2005;112 (4):412-7.*

5. *Kieler H, Zettergren T, Svensson H, Dickman PW, Larsson A. Assessing urinary albumin excretion in pre-eclamptic women: which sample to use? Br J Obstet Gynaecol 2003;110(1):12-17.*

6. *Wallenburg HCS. Detecting Hypertensive Disorders of Pregnancy in: Chalmers I, Eukin M, Kileirse MJNC, Eds. Effective care in Pregnancy and Childbirth. (1989). Oxford University Press, 382-402.*

7. *Saudan PJ, Brown MA, Farrel T, Shaw L. Improved methods of assessing proteinuria in hypertensive pregnancy. Br J Obstet Gynaecol 1977;104(1):1159-64.*

8. *Irgens- Moller L, Hemmingsen L, Holm J. Diagnostic value of microalbuminuria in pre-eclampsia. Clin Chim Acta 1986;157:295-8.*

9. *Douma CE, Van der Post JA, Van Acher BA, BOERK, Koopman MG. Circadian variation of urinary albumin excretion in pregnancy. Br J Obstet Gynaecol 1995; 102(2):107-110.*

10. *Meyer NL, Mercer BM, Fredman SA, Sibai BM. Urinary dipstick protein: a poor predictor of absent or severe proteinuria. Am J Obstet Gynecol 1994; 170: 137-40.*

11. *Young RA, Buchanan RJ, Kinch RA. Use of the protein - creatinine ratio of a single voided urine specimen in the evaluation of suspected preeclampsia. J Fam Pract 1996;42:385-7.*

12. *Robert M, Sepandj F, Liston RM, Dooley KC. Random protein-creatinine ratio for the quantitation of proteinuria in pregnancy. Obstet Gynecol 1997; 90:893-5.*

13. *Yamasmit W, Charoenvidhya D, Chaithongwongwattana S, Wongkitisophon K, Uerpairojkit B. Correlation between random urinary protein-to-creatinine ratio Quantitative estimation of 24 hour proteinuria in preeclampsia. J Med Assoc Thai 2003;86:69-73.*

14. *Thompson DR, Lieberman ES. Use of a random protein-to-creatinine ratio for the diagnosis of significant proteinuria during pregnancy. Am J Obstet Gynecol 2001; 185:808-11.*

15. *Ragip AA, Baykal A, Karacay O. Random urine protein-creatinine ratio to predict proteinuria in new onset mild hypertension in late pregnancy. Obstet Gynecol 2004; 104:367-71.*

16. *Durnwald C, Mercer B. A prospective comparison of total protein/creatinine ratio versus 24 hour urine protei in women with suspected preeclampsia. Am J Obstet Gynecol; 2003;189:848-52.*

17. *Cundy TF, Nixon D, Berkahn L, Baker J. Measuring the albumin excretion rate: agreement between methods and biological variability. Diabet Med 1992;9(2):138-143.*

18. *Higby K, Suiter CR, Phelps JY, Siler-Khodr T, Langer O. Normal values of urinary albumin and total protein excretion during pregnancy. Am J Obstet Gynecol 1994; 171:984-88.*