

## A comparison between urea reduction ratio and urea kinetic model in assessing hemodialysis adequacy in end stage renal disease

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### Abstract

**Introduction:** In recent years the burden of chronic kidney disease has increased worldwide. End Stage Renal Disease (ESRD) needs Hemodialysis as a common renal replacement therapy to reduce its morbidity and mortality. Hemodialysis adequacy must be maintained for effective treatment and is measured either by Urea Kinetic Model (Kt/V), Urea Reduction Ratio (URR), natural log Kt/V or Daugirdas 2<sup>nd</sup> generation formula. Though Kt/V is accurate, URR is commonly used in clinical practice because of its simplicity and clear concept.

**Objective:** To estimate and compare URR with single pool Kt/V in assessing hemodialysis adequacy.

**Materials and Methods:** An experimental prospective study consisting of 100 ESRD patients of either sex between 18-70 years, who were on hemodialysis maintenance. Blood urea was estimated by GLDH- urease method and serum creatinine by Jaffe's method. Values were substituted in URR and Kt/V formula.

**Results and Conclusion:** There was a significant difference in serum Urea levels after dialysis treatment ( $P < 0.05$ ). The values of URR and kinetic model of urea (Kt/V) were near to adequacy guidelines set by National Kidney Foundation: KDOQI. URR showed positive correlation with Kt/V. Since the URR and Kt/V are closely related, their predictive power in terms of patient outcome is similar. However, use of Kt/V and urea modelling allows for comparing expected with predicted dialysis dose that can be used to analyse dialysis treatment and dialyzer clearance.

**Keywords:** Urea reduction ratio, Kt/V, ESRD, Hemodialysis adequacy, Renal Dialysis, Urea.

### Introduction

Chronic kidney disease (CKD) is an important emerging chronic disease globally.<sup>1</sup> Chronic kidney disease and end stage renal disease (ESRD) place an immense strain on the health-care system in the society. But the exact magnitude of the burden of chronic kidney disease or end stage kidney disease is not known.<sup>2</sup> Prevalence is estimated to be 8-16% worldwide.<sup>3</sup> An Indian population-based study determined the crude and age-adjusted ESRD incidence rates at 151 and 232 per million population respectively.<sup>4,5</sup> and annually more than 100,000 new patients are entering renal replacement programs in India.<sup>6</sup>

CKD encompasses the spectrum of different pathophysiological process lasting for more than 3 months, associated with progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma and a progressive decline in GFR, eventually terminating in death when sufficient numbers of nephrons have been damaged. Leading causes of CKD includes diabetes mellitus, glomerulonephritis, hypertension, nephropathy, autosomal dominant polycystic kidney disease. Diabetic glomerular disease is the major cause of CKD (31.2%) in India.<sup>7</sup>

Based on clinical guidelines of National Kidney Foundation-Kidney Disease Outcomes Quality

Initiative(NKF/KDOQI), ESRD represents 5<sup>th</sup> stage of CKD with GFR  $< 15 \text{ mL/min/1.73m}^2$ . There is accumulation of toxins, fluids and electrolytes which are normally excreted by kidneys and disturbances in the nutritional status resulting in uremic syndrome. This affects virtually every organ system leading to death. Hence, hemodialysis as one of the renal replacement therapies can reduce the incidence of morbidity and mortality in patients with ESRD.<sup>7</sup>

Hemodialysis (HD) is based on law of diffusion and is targeted at removing both unwanted low and high molecular weight solutes and maintains equilibration of desired solutes. Hence, urea is a small molecule with substantial clearance. Also urea levels correlate with symptoms and well being. Efficiency of dialysis is also determined by blood & dialysate flow through the dialyzer as well as dialyzer characteristics. Even clinical indexes like good natural health, good regulation of arterial pressure, liquid balance & absence of uremic symptoms may be considered for effective HD thereby dose of dialysis is adjusted by knowing its efficacy to maintain the effective treatment.<sup>8</sup>

The mathematical indices like Kinetic model of urea (UKM) Kt/V, Urea reduction ratio (URR), Natural log Kt/V and Daugirdas 2<sup>nd</sup> generation formula are used to measure HD adequacy.

UKM- Kt/V is dimensionless formula introduced by Gotch F. & Sargent J. (1985) during the revision of National Cooperative Dialysis Study (NCDS)<sup>9</sup> where,

K is blood flow through dialysate (ml/min), t is duration in minutes and V is the volume of urea distributed & total body water (ml). In this we have different types as Single pool (Sp), Equilibrated (eKt/V) & Weekly standard (stdKt/V). URR is percentage reduction in urea levels given by the formula<sup>8</sup>

$$\text{URR} = \frac{\text{pre dialysis urea} - \text{post dialysis urea}}{\text{Pre dialysis urea}} \times 100$$

Natural log Kt/V,  $\text{Log}(e)^a = x$  where, e is natural logarithm base number;  $e = 2.718$ , a is real number to be converted to natural log, x is power that e must be raised to achieve a.<sup>10</sup>

Daugirdas 2<sup>nd</sup> generation formula,  $\text{Kt/V} = -\ln(R - 0.008 \times t) + (4 - 3.5 \times R) \times \text{UF/W}$  where  $R = 1 - \text{URR}$ .<sup>11</sup>

According to the guidelines set by National Kidney Foundation/Kidney Dialysis Outcomes Quality Initiative (NKF/KDOQI) (2006): Recommendation for 3 times / week frequency<sup>12</sup> to achieve Target spKt/V = 1.4; minimum spKt/v = 1.2 per dialysis and URR 70%; minimum URR = 65% per dialysis. These are measured monthly and it is an average rather than single value.<sup>13</sup> Dialyzer membrane should be high flux, biocompatible semipermeable membrane.<sup>14</sup>

Kt/V index is considered as prevailing accurate index/ marker of HD adequacy. Though Kt/V is accurate, URR is commonly used in clinical practice because of its simplicity and clear concept. Hence, the present study was conducted to see Hemodialysis adequacy by these two methods and to compare between them.

## Materials and Methods

The study was conducted in dialysis unit, Department of nephrology, Karnataka Institute of Medical Sciences, Hubballi as an experimental prospective study consisting of 100 ESRD patients on maintenance HD (> 6 months duration). Sample size was selected as a convenient size since exact prevalence of the disease is unknown. The study period was for one year (2014 July - 2015 June). It included age group of 18-70 years of either sex, maintaining the dose prescription of frequency three times per week. The dialyzer membrane used for the dialysis was polysulfone (Fresenius F6) and dialyzer size was 1.3m<sup>2</sup>

The Exclusion criteria were those ESRD patients who showed persistent non-compliance with their dialysis therapy, who did not receive their prescribed dialysis dose and those diagnosed with hepatic diseases.

Ethical clearance was obtained from the ethical committee. Detailed history was taken and patients were examined. After informed consent, 2 ml of blood was collected from arterial blood port connected to the patients, before and immediately after the dialysis in the same treatment session<sup>8, 15, 16</sup>. Serum was separated and Blood urea was estimated by GLDH- urease method

and serum creatinine by Jaffe's method<sup>17</sup>. Blood flow rate, duration of dialysis and weight of each patient noted. Values of collected data and biochemical data were used to calculate URR and Kt/V according to the formula.

## Statistical analysis

Statistical analysis was done using IBM SPSS version 19 Software, student 't' test was applied to test the hypothesis and Pearson Correlation to compare between URR and Kt/V. 95% confidence interval was applied and P value < 0.05 was considered statistically significant.

## Result

Table 1 show maximum patients were hypertensive in the study subjects.

A very high significant change observed in the values of blood urea and serum creatinine after dialysis with P value < 0.001 (Table 2).

In the present study, number of patients attending HD adequacy by URR of  $\geq 65\%$ , 64.9 to 55% and  $< 55\%$  were 39%, 34% and 27% respectively. 71% patients achieved spKt/V of  $\geq 1.2$  and 29%  $< 1.2$  Good number of patients received adequate hemodialysis treatment.

Table 3 and Graph 1 shows that URR can be correlated with Kt/V as the maximum no. of patients having URR  $\geq 65\%$  were attending Kt/V  $\geq 1.2$

URR is more consistent in its value than Kt/V (Table 4) as covariance is less than Kt/V.

Positive correlation was observed between URR and UKM ( $r = 0.415$ ) at 95% confidence interval (Table 5 and Graph 2).

## Discussion

In our study significant changes were observed in urea and creatinine levels after the dialysis. Study comprised of more males (68%) than females (32%) which was similar to the findings of Ajay K. Singh et al. in their study<sup>18</sup>. Hypertension was most common cause (43%) followed by diabetes mellitus in the present study. Similar study by A.S. Levey, et al. showed hypertension as a common cause followed by diabetes and CVD.<sup>19</sup> But Vivekanand Jha et al. showed glomerulonephritis as leading cause, followed by diabetes and hypertension in their study.<sup>2,3</sup>

Maximum patients received adequate dialysis treatment with URR > 55% and Kt/V  $\geq 1.2$ , near to the guidelines set by NKF: KDOQI. URR was more consistent than Kt/V. Hence it is more informative. Adrin Covic et al., conducted study on various methods of Kt/V and concluded that there are several methods of measurements of Kt/V which showed different results & stated that the concept of clearance is difficult to explain.<sup>20</sup>

URR showed high positive correlation with Kt/V in our study. Kailash Jindal et al. in their study tried linear regression analysis to evaluate the degree of correlation between Kt/V and URR and succeeded in achieving a simple and accurate method to estimate Kt/V using URR as there was positive correlation. He also states that URR is arithmetically straight forward & is an easily understandable concept.<sup>21</sup>

A study by V Kovacic showed similar URR (62.0±8%) and Kt/V (1.23±0.3) and found positive significant correlation (r=0.399) at P <0.001 between URR and efficacy quotient (Kt/V Daugirdas / Kt/V UKM).<sup>22</sup> Another study by Philip J. Held et al. showed close correspondence between Kt/V and URR for mortality assessment as there was high correlation between them (r=0.96).<sup>23</sup>

Few pitfalls of URR and Kt/V are URR is a measure of solute clearance only, without considering ultrafiltration where Kt/V is an accurate measure of both ultrafiltration and urea production but difficult and tedious to calculate and understand its clearance. Solute removal is perhaps a better way of clearance to quantify dialysis. If blood & dialysate flow rate are kept

constant, clearance during the first hour of dialysis will be the same as that of the last hour. But blood urea concentration is at its highest at the beginning of dialysis and solute removal will be much greater during the first hour than during the last hour. URR takes this into account but with Kt/V calculations all clearance are equal regardless of the amount of solute removal. V in Kt/V varies according to the patient's built (body surface area) of either sex i.e., smaller the patient, lower the value of V and more is the Kt/V. Hence it is falsely interpreted. Duration of the dialysis sampling gives different values. So, the correct beginning is when the blood flow is maximized and the post dialysis sample is collected immediately when the saline rinse begins to get accurate URR & Kt/V.

Since the concept of measurement of hemodialysis adequacy is complicated and is mathematically based, this study was an attempt to evaluate the efficacy of dialysis by simple methods at our hospital. Limitations of the study were dietary history as it was not satisfactory and single session sampling was done instead of average.

**Table 1: Co-morbidity causes for CKD/ESRD**

Co-morbidity	No. of patients (n)	Percentage (%)
Diabetes mellitus per se	14	14
Hypertension per se	43	43
Both Diabetes & hypertension	13	13
Cardiac diseases	09	09
Diabetes, hypertension and others like BPH etc.	10	10
Glomerulonephritis	07	07
Others	04	04

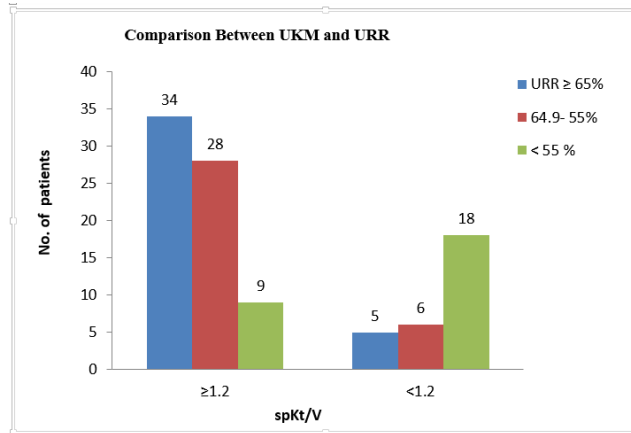
**Table 2: Pre and Post dialysis Blood Urea and Serum Creatinine**

Parameter	Pre dialysis mean(mg/dl)	Post dialysis mean(mg/dl)	Paired t test mean(mg/dl)	Standard deviation	p value
Urea	110.5	41.5	69.015	30.60	0.000
Creatinine	8.28	3.69	4.58	2.25	0.000

**Table 3: Comparison between UKM and URR**

Kt/V \ URR (%)	URR (%)			Total
	≥65	64.9 – 55	<55	
≥1.2	34	28	09	71
<1.2	05	06	18	29
Total	39	34	27	100

**Graph 1: Comparison between UKM and URR**



**Table 4: Hemodialysis Adequacy methods**

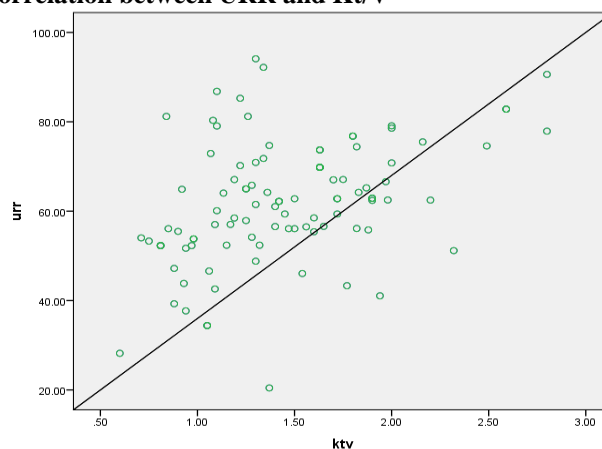
HD adequacy method	Mean ± SD	Covariance
URR	62.10 ± 13.72	22.09
Kt/V	1.45 ± 0.47	32.37

**Table 5: Pearson positive correlation between URR and Kt/V**

	Correlations (r)	URR	Kt/V
URR	Pearson Correlation	1	.415**
	Sig. (2-tailed)		.000
	N	100	100
Kt/V	Pearson Correlation	.415**	1
	Sig. (2-tailed)	.000	
	N	100	100

\*\* . Correlation is significant at the 0.01 level (2-tailed).

**Graph 2: Pearson positive correlation between URR and Kt/V**



r = 0.415\*\*

**Conclusion**

We found that maximum patients achieving HD adequacy have met and few have nearly met the KDOQI guidelines for URR & UKM and also observed a close relation between them which reflects their predictive power in terms of patient outcome. The results of URR were consistent. Hence it can be used as

measure of HD adequacy at the bedside in the clinical practice.

However, the use of Kt/V & urea modelling in general allows for comparing the expected dose of dialysis with the predicted dose, which can be used to analyze dialysis, dialyzer clearance and in troubleshooting & quality control activities.

## References

1. Ruggenenti P, Schieppati A, Remuzzi G: Progression, remission, regression of chronic renal diseases. *Lancet* 2001;357:1601-08.
2. Vivekanand Jha. Current status of end-stage renal disease care in India and Pakistan. *Kidney International Supplements* 2013;3:157-60.
3. Vivekanand Jha, Guillermo Garcia-Garcia, Kunitoshi Iseki, Zuo Li, Saraladevi Naicker, Brett Plattner, Rajiv Saran, Angela Yee-Moon Wang, Chih-Wei Yang. Global Kidney Disease 3, chronic kidney disease: Global dimension and perspectives *Lancet* 2013;382:260-72.
4. Jha V. Incidence of ESRD in India. *Kidney International* 2011;79:573.
5. Modi GK, Jha V. The incidence of end-stage renal disease in India: a population-based study. *Kidney International* 2006;70:2131-2133.
6. Kher V: End-stage renal disease in developing countries. *Kidney International* 2002;62:350-62.
7. Joanne M.B. and Karl Skorecki. Chronic Kidney Disease. In: Anthony S. Fauci, Dennis L. Kasper, Eugene Braunwald, Stephen L. Hauser, Dan L. Longo, J. Larry Jameson, Joseph Loscalzo, editors. *Harrison's Principles of Internal Medicine*. 18<sup>th</sup> edition. New York: McGraw Hill; 2012. chap 280. p.2308-21.
8. Sofia Zyga and Paul Sarafis. Hemodialysis adequacy-contemporary trends. *Health Science Journal* 2009;3(4):209-15.
9. Peter Kerr, Vlado Perkovic, Jim Petrie, John Agar and Alex Disney. Dialysis Adequacy (HD) Guidelines, Dose of hemodialysis. The CARI Guidelines-Caring for Australians with renal impairment 2005.
10. John R De Palma, Joanne D Pittard. *Dialysis Dose* Dec 04,2000.
11. John Daugirdas. Second Generation logarithmic estimates of single-pool variable volume Kt/V: An Analysis of Error. *J Am Soc Nephrol* 1993;4:1205-13.
12. Minimally adequate Hemodialysis. In: National Kidney Foundation 2006 updates Clinical Practice Guidelines and Recommendations. Guideline4. p.36-41.
13. Methods for measuring and expressing the hemodialysis dose. In: National Kidney Foundation 2006 updates Clinical Practice Guidelines and Recommendations. Guideline2. p.22-30.
14. Dialyzer membranes and reuse. In: National Kidney Foundation 2006 updates Clinical Practice Guidelines and Recommendations. Clinical Practice Recommendation5. p.81-6.
15. Methods for post-dialysis blood sampling. In: National Kidney Foundation 2006 updates Clinical Practice Guidelines and Recommendations. Guideline3. p.31-5.
16. Kailash Jindal, Christopher T. Chan, Clement Deziel, David Hirsch, Steven D.S., Marcello Tonelli and Bruce F.C. Chapter 1: Hemodialysis Adequacy in Adults. *J Am Soc Nephrol* 2006;17:S1-S27.
17. Edmund J. Lamb and Christopher P. Price. Kidney Function Tests. In: Carl A. Burtis, Edmund R. Ashwood and David E. Bruns. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. 5<sup>th</sup> edition. New Delhi: Elsevier publishers; 2012. chap25. p.669-701.
18. Ajay K Singh, Youssef MK Farag, Bharati Mittal, KK Subramanian, Sai Ram KR et al. Epidemiology and risk factors of chronic kidney disease in India-results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. *BMC Nephrology* 2013;14:114.
19. AS Levey, R Atkins, J Coresh, EP Cohen, AJ Collins, KU Eckardt, ME Nahas, BL Jaber, M Jadoul, A Levin, NR Powe, J Rossert, DC Wheeler, N Lameire and G Eknoyan. Chronic kidney disease as a global public health problem: Approaches and initiatives-a position statement from Kidney Disease Improving Global Outcomes. *Kidney International* 2007:1-13.
20. Covic A, Goldsmith D, Ken Hill, Venning M and Peter Ackrill. Urea Kinetic modelling-Are any of the bedside Kt/V formulae reliable enough? *Nephrol Dial Transplant* 1998;13:3138-46.
21. Jindal K. K., Manuel A and Goldstein M. Percentage reduction in blood urea concentration during HD(PRU). A simple and accurate method to estimate Kt/V urea. *ASAIO Trans* 1987;33:286-288.
22. V Kovacic. The assessment of hemodialysis technical efficacy. *Indian J Nephrol* 2004;14:1-9.
23. Philip J. Held, Friedrich K. Port, Robert A. Wolfe, David C. Stannard, Caitlin E. Carroll, John T. Daugirdas et al. The dose of hemodialysis and patient mortality. *Kidney International* 1996;50:550-6.