

# Urea Reduction Ratio as an Indicator of Dialysis Adequacy in Hemodialysis Patients

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## ABSTRACT

To compare the adequacy of hemodialysis by Urea Reduction Ratio in chronic kidney disease patients undergoing twice weekly hemodialysis with those undergoing thrice weekly dialysis. To compare the same in patients with comorbid conditions like cardiac failure, Hepatitis C Virus infection, hyponutrition, Diabetes & Hypertension. To analyse the influence of inter dialytic weight gain on URR in the same groups. Urea Reduction Ratio is adequate in thrice weekly hemodialysis patients when compared to twice weekly group. In patients with both diabetes and hypertension, URR was less than 65% in both thrice weekly & twice weekly dialysis patients. Hence patients with both diabetes and hypertension need better control and regular thrice weekly dialysis with longer duration. In patients with Hepatitis C Virus infection, even thrice weekly dialysis could not give adequate URR.

**Key words:** Hypertension, Diabetes, Dialysis, Hyponutrition

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## INTRODUCTION

Excretory function of kidney is affected in chronic kidney disease causing accumulation of most waste products produced in the body. One of the waste products easily measured is urea. Urea is mildly toxic, but high levels of urea indicate accumulation of more toxic waste products in blood and body that cannot be easily measured. These waste products can be removed from blood in kidney failure patients through dialysis. Dialysis has to be done frequently as waste products of metabolism keeps on forming continuously in the body. The adequacy of dialysis is measured periodically- usually once a month, by collecting blood at the beginning and at the end of dialysis. The levels of urea in both samples are compared. It is assessed by Urea Reduction Ratio. Urea reduction ratio is reduction in blood urea as a result of dialysis. This measures how effectively dialysis treatment removes waste products from the body.

Even though no fixed percentage can be said to represent adequate dialysis, patient has less complication, fewer hospitalisation & live longer if URR is at least 60%, so experts recommend a minimum URR of 65%. URR is measured after every 12 to 14 cycles of dialysis, which comes to once a month as most of the patients undergo dialysis twice or thrice a week. URR is percentage of reduction from the predialysis urea level. Average should

exceed 65%. Urea reduction ratio (URR) is used because the relative decrease in urea concentration during dialysis is the most significant determinant of fractional urea clearance represented by  $Kt/V$ , where K is the dialyzer urea clearance (expressed in liters per hour), t is time on dialysis (expressed in hours), and V is the volume of distribution of urea (expressed in liters). So direct measurement of URR has been proposed a simpler substitute for more complex equations to calculate dialysis dose.

This study compares the URR of renal failure patients undergoing hemodialysis twice a week versus hemodialysis done thrice a week. The influence of hyponutrition (as evidenced by concentration of albumin), and interdialytic weight gain over URR in both groups is also analysed. Other comorbid factors like hypertension, Diabetes mellitus, cardiac dysfunction, & hepatitis C virus infection were also taken for comparison.

## MATERIAL AND METHOD

Dried 50 Renal failure patients undergoing hemodialysis in Nephrology unit in Sree Balaji Medical College and Hospital were included in the study with age ranging from 15 to 75 years. Informed consent was obtained from the patients to do the study. The patients were divided into two groups depending on the number of dialysis session per week as twice weekly or thrice weekly. Urea, Creatinine, Albumin, blood glucose was taken in the Pre dialysis blood sample. Half an hour after dialysis was completed, blood- was taken and urea was repeated in the

patients. Inter dialytic weight gain was taken in all the patients. (The weight is taken after a dialysis session. Weight is again taken before the next dialysis and difference between the two is interdialytic weight gain). It was divided into three groups. (weight gain less than 2Kg, 2- 4Kg and more than 4Kg.) Written informed consent was obtained from all patients. Profoma with detailed history was taken.

### Inclusion criteria

Associated Diabetes Mellitus, Hypertension were included. Cardiac Failure was classified as mild, moderate & severe as per the echocardiogram done. Serum Albumin less than 3.5gm/dl was included for hyponutrition. Hepatitis C Virus infection were also included.

### Exclusion criteria

Chronic Kidney Disease patients with acute complications were excluded from the study. Patients who had started dialysis recently (less than three months) were also excluded. Urea Reduction Ratio was calculated & compared between the twice weekly dialysis & thrice weekly dialysis groups. Advantage of this ratio is that it can be done in hospitals in any area. There is no need for any costly equipments. It is cost effective, so all patients can afford it to know the adequacy of treatment.

### Method of assay

In 1993, Marshall devised a method for estimation of urea consisting of hydrolysis by urease, followed by

titrimetric estimation of ammonia. A gasometric method was established by Van Slyke in 1914 on a similar principle of hydrolysis of urea. Colorimetric estimation of ammonia was made possible by Nessler's reagent. But, this method involved deproteinization and posed turbidity problems at higher levels of urea concentrations. Subsequently, coupling of urease method with Berthlot reaction eliminated these problems and increased sensitivity may folds, earlier versions of Urea-Berthlot reaction used four reagents. In 1962, Chaney and Marbach modified the method by combining reagents to make it a three reagent system and simplified the technique. Use of sodium salicylate instead of phenol and the use of sodium nitroprusside as an accelerator has improved performance of the reagent system making it a two reagent systems.

### RESULTS

A Results were analysed by using SPSS 15 software.

Total number of patients were 50 of which there was 30 males and 20 females. Twice weekly dialysis group comprised of 28 patients. Thrice weekly dialysis group comprised of 22 patients. Overall 70% of patients had URR less than 65%. When Urea Reduction Ratio was compared between twice weekly & thrice weekly group, it was statistically significant as shown in table 1. (student t-test P-value 0.000)

**Table 1: URR between twice weekly and thrice weekly dialysis groups.**

URR Percentage	N	Mean	Std. Error Mean	T-Value	P-Value
Twice weekly Thrice weekly	28	53.3036	1.14631		
	22	67.8	1.58052	7.607	0.000 (S)

N=50. (S) = Significant When URR is compared between two groups by graph, (graph 1&2), there is significant reduction in URR in twice weekly dialysis group and more decrease in urea after dialysis in thrice weekly

group. WITHIN THE GROUPS: (twice weekly group & thrice weekly group). Though there was reduction in URR between subgroups within the main group, it was not statistically significant.

**Table 2: URR between HCV + & HCV - in thrice weekly dialysis.**

URR Percentage	N	Mean	Std. Error Mean	T-Value	P-Value
HCV+	4	67.8	2.91919		1
HCV-	18	67.8	1.85402	0	(NS)

HCV- Hepatitis C Virus, NS = Not significant

**Table3: HCV + & HCV - in twice weekly dialysis.**

URR Percentage	N	Mean	Std. Error Mean	T-Value	P-Value
HCV+	4	57.65	0.46547		0.124
HCV-	24	52.5792	6.2714	1.591	(NS)

**Table 4: URR & Albumin <3.5g/dl & above 3.5g/dl in thrice weekly dialysis.**

URR Percentage	N	Mean	Std. Error Mean	T-Value	P-Value
Albumin< 3.5g/dl	7	65.4857	1.97682		0.329
Normal >3.5g/dl	15	68.88	2.11005	1	(NS)

**Table5: URR & Albumin <3.5g/dl & >3.5g/dl in twice weekly dialysis.**

URR Percentage	N	Mean	Std. Error Mean	T-Value	P-Value
Albumin< 3.5g/dl	12	52.7417	2.10876	-418	0.679
Normal> 3.5g/dl	16	53.725	1.29066		(NS)

**Table 6: URR in patients with Diabetes, Hypertension & with both Diabetes and hypertension in thrice weekly dialysis.**

URR Percentage	Sum of Squares	Df	Mean Square	F value	Sig.
D,HT,D&HT.					
Between groups	61.578	3	20.526	0.338	0.798
Within Groups	1092.522	18	60.696		(NS)
Total	1154.1	21			

D = Diabetes Mellitus, HT = Hypertension,

**Table7: ANOVA Table Comorbid conditions with in twice weekly dialysis group.**

URRpercentage	Sum of squares	Df	Mean square	F value	Sig.
D, HT, D & HT					
Between groups	25.753	3	8.584	0.213	0.886
Within groups	967.657	24	40.319		(NS)
Total	993.41	27			

**Tables 8: ANOVA Table Cardiac failure: mild, moderate & severe in thrice weekly dialysis.**

URR Percentage	Sum of Squares	Df	Mean Square	F value	Sig.
CARDIAC FAILURE (mild, moderate & severe)				1.3	.305 (NS)
Between groups Within Groups					
Total			68.492		
	205.477	3	52.701		
	948.623	18			
	1154.1	21			

Table 9: ANOVA Table URR &amp; cardiac failure in twice weekly dialysis.

URR Percentage	Sum of Squares	Df	Mean Square	F value	Sig.
CARDIAC FAILURE (mild, moderate & severe)				0.83	0.49
Between groups			31.128		(NS)
Total	93.385	3	37.501		
	900.025	24			
	993.41	27			

Table 10: Interdialytic weight gain in thrice weekly dialysis.

URRpercentage	Mean	N	Std. Deviation	Std. Error of Mean	F value	Sig.
Less than 2Kg	67.48	5	4.5975	2.05606		
2-4Kg	68.21	10	8.91945	2.82058		0.975
More than 4Kg	67.4429	7	7.64261	2.88864	0.025	(NS)
Total	67.8	22	7.41331	1.58052		

Tables 11: URR percentage &amp; interdialytic weight gain with in twice weekly dialysis

URRpercentage	N	Std. Deviation	Std. Error of Mean	F value	Sig.
Less than 2Kg	8	7.09039	2.50683		
2-4Kg	15	4.2861	1.10667		0.115
More than 4Kg	5	7.52728	3.3663	2.358	(NS)
Total	28	6.065572	1.14631		

Table 12: URR for HCV + between twice weekly and thrice weekly dialysis group.

URR Percentage	Mean	Std. Error Mean	T-Value	P-Value
Twice weekly	57.65	0.23274		0.013
Thrice weekly	67.8	2.91919	3.466	(S)

**Table 13: URR for albumin <3.Sgm/dl between twice weekly and thrice weekly dialysis group.**

URR Percentage	N	Mean	Std. Error Mean	T-Value	P-Value
Twice weekly	12	52.7417	2.10876	4.031	.0001 (S)
Thrice weekly	7	65.4857	5.23018		

## DISCUSSION

Dialysis adequacy is related to mortality and morbidity in renal failure patients on hemodialysis. Improvement in mortality have been associated with improvement in Urea Reduction Ratio. Hence assessment of adequacy of dialysis by monthly URR is simple test to control morbidity and mortality. URR is shown to be comparatively less in males than in females. This may be due to the lower body mass in females [10]. As dialysis is prescribed without taking this into account, females tend to have more URR. This study does not show significant difference in URR between males and females. In this study more number of patients preferred to have twice weekly dialysis even though they were advised to have thrice weekly dialysis. This was due to the financial constraints and other problems like dependence on others to take them to hospital etc. The URR of these patients were less than 65%. The same was noted in Iranian multicentric study [16] where URR was less than 65% in more than 50% of patients studied. Patients with serum albumin less than 4gm/dl have increased mortality. This was shown in a retrospective study by William. F. Owen et al. In our study serum albumin was less than 4gm/dl in majority of patients. Hence care should be taken to improve the nutrition of patients undergoing hemodialysis by giving protein rich diet. Inadequate nutrition has an impact on mortality is shown by numerous studies in various countries. Their study in Manipal Bangalore had concluded that economic status in India varies and management of End Stage Renal Disease depend on individual patient's paying capacity. In our study too financial problem was the reason for more number of twice weekly dialysis even though they were advised to have thrice weekly dialysis which resulted in reduced URR. In the above study by H. Sudarsan Balal et al, a lower dialysis dose was not correlated with serum albumin, but in our study patients had lower serum albumin probably due to inadequate protein intake.

gain is directly associated to better nutrition status. Beneficial effects were greater than negative aspects that depend on blood pressure. Weight gain may be due to increased water retention in hypertensive patients or because of insufficient removal of fluid during dialysis. In the present study weight gain of 2Kg & 2-4 Kg had good URR compared to weight gain of >4 Kg. HCV infection is higher than in general population. It is mainly transmitted by nosocomial transmission. Universal sanitary precautions prevent transmission. In our patients with HCV infection there is reduced URR even in thrice weekly group. Non-diabetics had better URR than diabetics as shown 101 Our patients with both

Hypertension and Diabetes had lower URR even in thrice weekly dialysis. Hence they should be treated with proper drugs and evaluated periodically. Within twice weekly group, URR is less in all the categories. Hence dialysis is not adequate for these patients. With in thrice weekly group, URR is good in majority of the patients. But even in thrice weekly dialysis URR is not adequate in patients suffering from combined Diabetes and hypertension. This may be due to less residual kidney function in these patients so they may need longer duration of dialysis. Hepatitis C Virus positive patients also have less URR in thrice weekly group. Moderate & severe cardiac failure patients and patients with interdialytic weight gain above 4 kg too have less URR in thrice weekly group may be due to excess water retention and electrolyte imbalance. Hence these patients need extra care and attention towards treatment of comorbid conditions, with longer duration of dialysis.

## CONCLUSION

In conclusion we can say that in renal failure patients on hemodialysis, it is mandatory to do thrice weekly dialysis for all patients so as to get good control and decrease morbidity and mortality. In our country where dialysis is costly all patients cannot afford to have thrice weekly dialysis regularly. We need to make hemodialysis cost effective, so that all patients can get adequate dialysis irrespective of socioeconomic status. Thrice weekly dialysis need to be promoted to all patients on long term dialysis to prevent morbidity and have comfortable life. URR which is a very simple test should be done periodically to know dialysis adequacy in all patients in any setting.

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## DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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