Assessment of Dialysis Adequacy Using Urea Reduction Ratio and *KT/V* in four Pediatric Hemodialysis Centers in Baghdad

Ali Ahemd, Nariman F.Ahmed Azat, Shatha Ali

ABSTRACT:

BACKGROUND:

The 21st century has been set to enhance dialysis adequacy. Numerous studies have confirmed the association between the delivered dose of hemodialysis and patients outcomes. There is thus some evidence regarding the relationship between dialysis dose and quality of life.

OBJECTIVE:

To assess dialysis adequacy using (Urea Reduction Rate and *KT/V),* and to determine the association between dialysis dose and different Hemodialysis characteristics in children with End Stage Renal Failure undergoing Hemodialysis.

METHOD:

This was an observational cross-sectional study that was conducted for three months, from (November 2014 till January 2015); we enrolled 50 children with End Stage Renal Failure in four hemodialysis centers in Baghdad. Samples for blood urea (predialysis and postdialysis) were drown to calculate the adequacy dose.

RESULTS:

Thirty two (64%) of patients were male and 18(36%) were females; with male to female ratio was (1.7:1).The mean urea reduction ratio and Kt/V were 59.63 ± 7.345% and 1.29 ± 0.275, respectively, with fair dialysis adequacy .A Kt/V less than 1.2 and a urea reduction ratio less than 65% were found in 42%, and 38% of the hemodialysis patients, respectively. There was a significant correlation between dialysis dose and (Blood flow rate, Dialysis hours, Dialysis frequency /week and Effective surface area), while there was insignificance correlation with (gender, age, volume of ultrafiltration.

CONCLUSION:

Our results were better than neighbor countries with fair dialysis adequacy. It is important to regularly measure the parameters of dialysis adequacy in order to assess whether targets are achieved in accordance with K/DOQI guidelines.

KEY WORDS: adequacy ,hemodialysis,children

INTRODUCTION:

There are about 1.8 million patients with (ESRD) all over the world that need a kind of renal replacement therapy (RRT).[1]

The 21st century has been set to enhance dialysis adequacy, in attempts to improve patients' quality of life. World- wide, currently more than 500 000 people are undergoing hemodialysis treatment. [2]

The National Cooperative Dialysis Study established that greater the efficiency of dialysis, lesser is the mortality and complications of uremia. [3]

*Children Welfare Teaching Hospital,
**Medical College of Baghdad,
***Al-Nahrin College of Medicine,

Assessment of adequacy: [4]

For practical reasons HD adequacy has been measured using small, easily measured solutes such as urea.

Two commonly used measures of HD adequacy are:

urea reduction ratio (URR) and Kt/V_{urea}

The URR is easy to perform and is the index of dialysis dose which is most widely used in the UK.

Single- pool Kt/V_{urea}*:* This method has been validated in major adult studies to predict morbidity. because it assumes that urea is removed from a single pool, a delayed postdialysis sample is not required. This is clearly a great practical advantage, and is the easiest to calculate

K: dialyzer clearance of urea; t: dialysis time; V: patients total body water.

The dialysis care team should deliver a Kt/V of at least 1.2 (single-pool, variable volume) for both adult and pediatric hemodialysis patients. [4]

AIM OF THE STUDY:

This study was designed to assess dialysis adequacy using (Urea Reduction Rate and *KT/V)and To determine the association between dialysis dose and different* Hemodialysis characteristics in four pediatric Hemodialysis Centers in Baghdad.

PATIENTS AND METHOD:

This was an observational cross-sectional study that was conducted for three months, from (November 2014 till January 2015), in four hemodialysis centers hospitals in Baghdad, to describe the relation between hemodialysis adequacy and various variations.

Study sample:

Randomly we enrolled 50 children with CKD on HD from four HD pediatric centers {Ibn Al-Balady Hospital 18 (36%), Child Central Teaching Hospital 16 (32%), Al-Kadhimiya Teaching Hospital 9(18%) and Al-Karama Teaching Hospital 7(14%)}. At the initiation of the study, 51 patients were enrolled. During the course of the study, one patient died because of cardiovascular complication of CKD during HD, and ruled out from the study. The studied samples (50 patients) attended HD unit and were on regular hemodialysis sessions according to special schedules of that hospital; patients who have been on maintenance hemodialysis for at least three months duration were considered for the study.

Informed consent was obtained from all the patients and /or their relatives with explaining the aim of the study.

Data Collection:

A preformed questionnaire had been used for patients in study group. It includes demographic data = names, ages, gender).

Enquiry about investigations included :(Blood Urea (hence BUN calculated), Serum Creatinine; other parameters recorded like height and surface area as needed; the weight and blood pressure obtained pre &intradialysis. While GFR calculated according to Schwartz formula [5].

Adequacy formulae: we use two famous formulae as follow:

Urea reduction ratio (URR): It is measured as follows:

URR= {(Predialysis BUN- Post dialysis BUN) ÷ Predialysis BUN} × 100

Kt/V $_{urea}$: In the study we use the *single- pool Kt/V only*: [6, 5]

The second-generation formula for estimating spKt/V, which was reported and validated by Daugirdas, is recommended. [6]

Kt/V $_{urea}$ was calculated using simplified formula of *Daugirdas*. [7]

$$spKt/V = -Ln\,(R - 0.008t) + (4 - 3.5R)\,UF/BW$$

K: Dialyzer urea clearance supplied by the manufacturer in liters per minute (l/min).

t: The duration of dialysis in minutes (min).

V: The volume of distribution of urea in liters (l).

Sp: Single pool

- ***Log n*** is the natural logarithm
- ***R*** is the *postdialysis BUN ÷ predialysis BUN*
- ***t*** is the length of the dialysis session in hours
- ***UF*** is the ultrafiltration volume in liters
- ***BW*** is the patient's *postdialysis* weight in kilograms

Methods for blood sampling:

The following points were considered in blood sampling collection

Both samples (predialysis and postdialysis) were drawn during the same treatment session.

The risk of underestimating predialysis BUN level because of saline dilution or by sampling the blood after treatment was avoided.

Stop dialysate flow technique: At the end of the dialysis time, dialysate flow was stopped but kept the blood pump running. After 5 min with no dialysate flow a blood sample was taken from anywhere in the blood circuit (i.e. the arterial or venous port), the withdrawal of (10-15cc) as dead space. Blood samples then centrifuged in order to obtain blood serum and hence the urea.

Statistical analysis:

Data were computerized using Microsoft Excel program 2010; statistical analysis was done using the (SPSS version 19) software for windows and the *t*-test and *chi* square were used to compare the means of different groups for continuous variables. Study confidence interval was 95%.

In the statistical evaluation, the following levels of significance are used**:**

Non-significant	NS	P > 0.05
Significant	S	0.05 ≥ P > 0.01
Highly significant	HS	P ≤ 0.01

RESULTS:

This study included 50 pediatric patients with end stage renal disease who were on maintenance hemodialysis.

***Gender*:** thirty two (64%) of patients were male and 18(36%) were females**.** male to female ratio was (1.7:1).

***AGE*:** the age of patients in the study group ranged between (4 years to 16 Years). Most of the patients (46%) were between the age group (10-15 years); only two patients (4%) were below 5 years old

URR& Kt/V in the study sample:

Table -1- the results of the current study showed that an acceptable number of patients were adequately dialyzed (p value were highly significant (0.000).

- 58% of patients (n=29) had Kt/V ≥ 1.2 (ranging from 1.21 - 2.28).
- 62% of patients (n=31) had URR ≥ 65%.

Table 1: Kt/V and URR % of the study sample

		Descriptive statistics					
		N	Mean	S.D.	Min.	Max.	p-value
Kt/V	< 1.2	21 (42%)	0.89	0.24	0.45	1.19	0.000 (HS)
	≥ 1.2	29 (58%)	1.57	0.31	1.21	2.28	
	total	50	1.29				
URR %	< 65	19 (38%)	52.29	8.22	35	64.98	0.000 (HS)
	≥ 65	31 (62%)	69.9	6.47	65	82	
	total	50	59.63				

2- correlation between Demographic data and prescribed dialysis dose (KTV and URR):Data presented in table (1) showed the various tested variables (age and gender) in association with adequacy of hemodialysis based on Kt/v and URR values. No significant differences found with respect to gender, and age among study population.

Table 2: Correlation between Demographic data and prescribed dialysis dose (KTV and URR).

Demographic data								
Variables		No. (%)	Kt/V			URR %		
			<1.2	≥ 1.2	p-value	< 65	≥ 65	p-value
			No. (%)	No. (%)		No. (%)	No. (%)	
Genders	Males	32 (64)	15 (71.43)	17 (58.62)	0.352 (NS)	13 (52.6)	19 (54.8)	0.157 (NS)
	Females	18 (36)	6 (28.57)	12 (41.38)		6 (47.4)	12 (45.2)	
Age (year)	< 5	2 (4)	0	2 (6.90)	0.410 (NS)	1 (5.2)	1 (3.2)	0.422 (NS)
	5-10	15 (30)	6 (28.57)	9 (31.03)		7 (36.8)	8 (25.8)	
	10-15	23 (46)	9 (42.86)	14 (48.28)		6 (31.7)	17 (54.8)	
	> 15	10 (20)	6 (28.57)	4 (13.79)		5 (26.3)	5 (16.2)	
Total		50	21	29		19	31	

3- Hemodialysis characteristics: Table (3) shows the following:

3-1 blood flow rate (BFR): the blood flow rates ranged from 100 (ml/min) to 350 (ml/min), most patients in our study 19 (38%) patients were dialyzed with (*BFR)* between 201-250ml/ min, among these patients 51.8% (N=15) patients had Kt/V ≥ 1.2, and 48.4 (N=15) patients had URR ≥ 65. The p value was highly significant in this group.

3-2 Dialysis hours: according to dialysis hours the patients were divided into 3 groups, most of them 35(70%) patients were dialyzed for 3 hours, from this group; 23(79.3%) patients had a Kt/V ≥1.2, and 25(80.6%) had a URR ≥65%, the patients who were dialyzed more than 3 hours were only 5(10%) patients and all of them were in good adequacy. The P value was significant.

3-3 Dialysis sessions per week: also the patients were divided into 3 groups, most of patients (70%) were dialyzed twice weekly, 20 (68.9%) patients had a Kt/V ≥1.2, and 22 (70.9%) patients had a of URR ≥65%. The P value was highly significant.

3-4 Volume of UF: 72% (N=36) of patients with UF between < 1liter/UF to >2liter /UF, and 9(18%) patients with no UF. The P value was not significant.

3-5 Effective Surface Area: we have 3 groups (0.8, 1and 1.2m^2), 26(56%) patients dialyzed with 1m^2, of those, 18 (62.1%) patients had a Kt/V ≥1.2, and 19 (61.3%) patients had a URR > 65%. Also the P value was significant.

Table 3: Hemodialysis characteristics.

Variables		No. (%)	Kt/V			URR %		
			<1.2	≥ 1.2	p-value	< 65	≥ 65	p-value
			No. (%)	No. (%)		No. (%)	No. (%)	
Blood Flow (ml/min)	100-150	11 (22)	9 (42.9)	2 (6.9)	0.004 (HS)	8 (42.1)	3 (9.6)	0.003 (HS)
	151-200	8 (16)	7 (33.3)	1 (3.4)		4 (21.1)	4 (12.9)	
	201-250	19 (38)	4 (19.1)	15 (51.8)		4 (21.1)	15 (48.4)	
	251-300	7 (14)	1 (4.7)	6 (20.6)		2 (10.5)	5 (16.2)	
	301-350	5 (10)	0	5 (17.3)		1 (5.2)	4 (12.9)	
Dialysis hours (hr.)	2	10 (20)	9 (42.8)	1 (3.4)	0.025 (S)	9 (47.3)	1 (3.2)	0.034 (S)
	3	35 (70)	12 (57.2)	23 (79.3)		10 (52.7)	25 (80.6)	
	> 3	5 (10)	0	5 (17.3)		0	5 (16.2)	
Dialysis session (weeks)	1	4 (8)	4 (19.1)	0	0.002 (HS)	3 (15.7)	1 (3.2)	0.003 (HS)
	2	35 (70)	15 (71.4)	20 (68.9)		13 (68.5)	22 (70.9)	
	3	11 (22)	2 (9.5)	9 (31.1)		3 (15.8)	8 (25.9)	
Volume of UF (L.)	No	9 (18)	5 (23.81)	4 13.79	0.579 (NS)	2 (10.5)	7 (22.5)	0.429 (NS)
	0-1	18 (36)	7 (33.33)	11 37.93		8 (42.2)	10 (32.3)	
	1.1-2	18 (36)	6 (28.57)	12 41.38		7 (36.8)	11 (35.5)	

	2.1-3	5 (10)	3 (14.29)	2 6.90		2 (10.5)	3 (9.7)	
Effective Surface Area (m^2)	0.8	19 (38)	9 (42.8)	10 (34.4)	0.032 (S)	8 (42.1)	11 (35.5)	0.012 (S)
	1	26 (52)	8 (38.1)	18 (62.1)		7 (36.8)	19 (61.3)	
	1.2	5 (10)	4 (19.1)	1 (3.5)		4 (21.1)	1 (3.2)	
Total		50	21	29		19	31	

DISCUSSION:

Increasing evidence demonstrates that mortality among ESRD patients is lower with sufficient hemodialysis treatments. [8]

The lack of published Data on hemodialysis practice in pediatrics in Iraq and For the potential impact of intervention required to improve this type of renal replacement modality.This study tried to highlight some of hemodialysis practices and associated findings for patients treated in four major pediatric hemodialysis centers in Baghdad.

Demographic data:

Adequacy and gender: the majority of ESRD patients in almost all countries are in males rather than females this gender distribution reflects the higher incidence of congenital disorders in boys versus girls that lead to ESRD .[9, 10] nationally conducted study, suggested that females were with a better response to clearance of uremia toxins, compared to males. [11] Our findings in this respect are consistent with various reports as males were represented by a higher percentage (64%) compared to females population (36%), and demonstrate a higher level of clearance among female population as 71.43% of the males were with Kt/V values (< 1.2), compared to 28.57% among females population, and (URR <65%)in male was 52.6% and female 47.4%, However, these variation were of no statistically significant values (p=0.352, and P=0.157 respectively).these finding goes with Allam study. [12]

Adequacy and age: 46% of our sample was between 10-15 years age group, and it is consistent to the Indian study with a median age of 13years old. [13] While median age in Doaa study in Egypt was 5.6years old and Turkish children were 9.5. [14] And this may reflect geographic variability in age of onset and the type of etiology of CKD in children, and, as we see later in this chapter. Difference in clearance rates among the various age groups were statistical insignificant (p=0.410, p=0.22) for Kt/V & URR, respectively.

-URR& Kt/V in the study sample:

According to the KDOQI guidelines for hemodialysis patients, the minimally adequate dose of dialysis should be a single-pool Kt/V of 1.2 or a URR of 65%, and the recommended target dose should be a Kt/V of 1.4 or a URR of 70%. [15]

In the current study the mean Kt/V and URR for the patients were 1.29± 0.275 and 59.63± 7.335, respectively, 58% of all patients achieved the Kt/V goal and 62% had target URR. These results were a little bit better than neighbor countries; in Iranian study the mean single-pool Kt/V and URR were 1.17 and 61%, respectively. [16] In Palestine the mean Kt/V and URR were 1.06 ± 0.05 and 54.4 ± 19.3, respectively. [17] While in Five European Countries and the United States as following:

Adequacy of Hemodialysis Compared With Five European Countries and the United States

Variable	France*	Germany*	Italy*	Spain*	UK*	USA†
Mean Sp Kt/V	1.51	1.30	1.32	1.32	1.38	1.55

* Based on the Euro-Dialysis Outcomes and Practice Patterns Study. [18]

† Based on the 2007 annual report of ESRD clinical performance measures project. [19]

The substantial discrepancy in hemodialysis adequacy between forementioned developed countries and Iran at least, to some extent, may be resulted from more frequent use of high-flux dialysis. While in our study we will see the different parameters that affecting the adequacy.

Hemodialysis characteristics:

***1-Blood flow rate*:** Blood flow is one of the principle determinants of dialyzer urea clearance and low blood flow rates lead to lower urea clearance. [20]

Blood flow rates affected by poor vascular access, recirculation, insufficient anticoagulation and human errors, some of these problems can be solved especially when it comes to vascular access. [21] In the current study blood flow rates clustered in five groups. Most of our sample 38% of them lie between 201-250 ml/min, similar finding in Al-Kadhimiya study. [22]

Increased blood flow rates found to be associated with increased rate of clearance. Our findings in this respect in consistent with previous reports that, indicates better clearance rates in association with increased flow rates. [16, 23]

2- Dialysis hours: There are numerous observational studies supporting the positive association between the length of hemodialysis session and survival rate. [24] Our finding, 70% dialyzed for 3 hours, of them 65.75% and 71.4% with good adequacy (Kt/V≥1.2, URR ≥65%, respectively), and all who dialyzed >3 hours with very good adequacy, (p=0.025, 0.034).this supported by Allam study [12], Laurent et.al. [25] It is important to note that patient's non-compliance, lack of enough dialysis machines and facilities and access to these facilities are major time limiting factors for dialysis.

3-Dialysis session per week: Studies have documented the relationship between less frequent dialysis per week and poorer outcome. [26] The majority of the study population (70%) was dialyzing twice times per week and 57.1% of them were with a Kt/v value of ≥ 1.2, and 73.3% with URR≥65%, by increasing the frequency of dialysis per week to thrice, the Kt/V&URR increased as well. This goes with agreement with Manouchehr A.et.al. [16], Allam [12], Mohamed et.al. [27] Differences in the clearance rates were statistically highly significant (Kt/V; p=0.002, URR; p=0.003).

4- Volume of UF: Few studies have examined the direct association of UF rate on long-term outcomes in HD patients. The Netherlands Cooperative Study on the adequacy of dialysis recently reported the association between excessive ultrafiltration and mortality, independent of delivered Kt/V urea. [28] Our findings with respect to ultrafiltration rate and clearance show a clear trend of improvements in Kt/V values and URR till 2 liter/UF and then decreased after more UF rate, this may be due to decrease sessions frequency (poor compliance, far address, poor socioeconomic status) with interadialytic fluid retention, and may lead to less dialysis efficiency. although this relation was statistically insignificant, unlike Allam findings [12] .

***5- Effective Surface Area*:** The use of larger surface area dialyzers permits high rates of urea clearance to be achieved offering theoretical advantage of improving blood purification by removing higher and middle molecular – weight solutes. [29] Furthermore, many studies reported excellent survival among patients treated with larger surface filter area, which in turn reflects to better dialysis adequacy. [30] With respect to filtration area, our study population placed on three different membrane size filters (0.8, 1 and 1.2m^2). When these groups compared with regard to their clearance rates, 62.1% of those who were on 1m^2 were with a Kt/v value of ≥ 1.2, 61.3% with URR ≥65%, compared to only 34.4% among those who were on 0.8m^2, and URR with 35.5%,and last small sample group (1.2m^2) was statistically negligible. Such finding is in agreement with previous reports on membrane size and clearance rates. [29,30]

CONCLUSIONS AND RECOMMENDATIONS

The dialysis adequacy using the (Kt/V and URR) in the current study was acceptable and the hemodialysis adequacy was influenced by several factors such as: Blood flow rate ,Dialysis hours per session ,Dialysis frequency per week and Effective surface area

We recommend regularly measuring dialysis adequacy on monthly bases in the dialysis units in order to determine what degree of enough dialysis the patients are receiving during their treatments and this should be a routine protocol and better registration and follow up.

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