Geget (20п) 11 (1 ¸ : 47 - бо
The Egyptian Society for Pediatric ephrology and Transplantation (ESPNT)

Original Article

Assessment of Hemodialysis Adequacy and Factors Affecting it in Pediatric Patients Using Single Pool Ю/ Г Equation in Zagazig University

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ABSTRACT

Background: Quantification of the dialysis dose is an essential element in the management of chronic hemodialytic treatment. Urea clearance is used as a marker of dialysis adequacy although urea only represents small readily permeable solutes but it has several advantages over other an uremic toxins. Several factors affect clearance and include the blood flow rate; the dialysate flow rate and the efficiency of the dialyzer. Other indicators of dialysis adequacy include the removal of large solutes as creatinine, vitamin B12 and B2 microglobulin and control of the extracellular volume and blood pressure. Adequacy of dialysis should be assessed in all patients at least 3 monthly as clinically based assessment has proven unreliable.

Objectives: The aim of this study is to assess hemodialysis adequacy and factors affecting it in pediatric patients in pediatric nephrodialysis unit in Zagazig University.

Methods: This study was carried out in pediatric nephrodialysis unit in Zagazig University. It included 30 patients with chronic renal failure on regular hemodialysis. The studied group included 18 females and 12 males. Their ages ranged from 6 to 20 years. They were regularly hemodialysed 3 times weekly and 2 to 4 hours per session by polysulfone membrane using citrate dialysate and their pump rate ranged from 180 to 200 ml/minute. All of them had arteriovenous fistulae. All cases were subjected to detailed history taking, thorough clinical examination and laboratory investigations. Blood urea level pre and post dialysis session using urease colorimetric method was done. Assessment of single pool KdV using the following equation:

Kt/V = 2.2 - 3.3 X (u post/u pre - 0.03 - (w pre — w post)/w post).

Results: We found a significant positive correlation between Kt/V and pump rate, surface area of the dialyzer and duration of dialysis. A highly significant positive correlation was found between Kt/V and dialysis session length and also with serum albumin. No significant correlation was found between Kt/V and other laboratory parameters or blood pressure. The most effective parameter affecting the dialysis efficiency is the dialysis session length.

Conclusion: We conclude that adequate dialysis maximizes well-being, minimizing morbidity, and helps a patient retain social independence. Dialysis prescription should be individualized, monitored, and reassessed regularly. Improving dialysis adequacy as indicated by increased Kt/V can be achieved by increasing dialysis session length, pump rate and the size of the dialyzer.

INTRODUCTION

With dialysis and renal transplantation as long-term renal replacement therapy (RRT), the prognosis of end stage renal failure in children has been completely changed[1]. The main aims of dialysis treatment are to prolong _patient survival, reduce morbidity and improve quality of

lifet[2]. Since inadequate dialysis increases mortality and morbidity of patients, therefore, assessment of dialysis adequacy is clinically importantt[3]. Adequate delivered dose of solute removal is assessed by urea reduction and calculation of KtN. The most useful and widely applied index to prescribe the dialysis dose (as well as to assess the dose which is actually delivered) is the KtN[(4)]. Urea reduction ratio (URR) continues to be viable but with pitfalls. Although URR correlates well with spKtN in population studies, significant variability in correlation in individual patients occurs because URR fails to include both the contraction in extracellular volume (ECV) and the urea generation that typically occur during routine hemodialysis (HD)[(5)]. The urea reduction ratio (URR) is calculated from the difference in the blood urea concentration before and after dialysis divided by the pre-dialysis blood urea concentrationt[6)]. Delivered HD dose (Kt/V) value is calculated by various formulae utilizing pre- and postdialysis blood urea concentrations. The Kt/V value represents dialyzer clearance (K) distribution volume of urea (V) and dialysis duration (t)[(7] . Current guidelines suggest a minimum Kt/V of 1.2 for three weekly hemodialysis sessions[(^)].

AIM OF THIS STUDY

The aim of this study was to assess hemodialysis adequacy and factors affecting it in pediatric patients in the Pediatric Nephrodialysis Unit in Zagazig University.

PATIENTS AND METHODS

This study was carried out in the Pediatric Nephrodialysis Unit in Zagazig University. It included 30 patients with chronic renal failure on regular hemodialysis. The studied group included 18 female and 12 males. Their ages ranged from 6 to 20 years. They were regularly hemodialysed 3 times weekly and 2 to 4 hours per session by polysulfone membrane using citrate dialysate. Their pump rate ranged from 180 to 200 ml/minute. All of them have arteriovenous fistulae.

All patients in this study were subjected to full history taking, through clinical examination, laboratory investigations including complete blood count. serum albumin, creatinine, calcium, phosphorus, serum iron, ferritin, parathyroid horuione, partial thromboplastin time and prothrombin time. Blood urea level using urease colorimetric method. Assessment of single pool Kt/V using the following equation:

Kt/V 2.2 - 3.3X (u post/u pre - 0.03 - (w pre - w post)/w post)[(9] .

U pre = pre-dialysis urea.

U post = post-dialysis urea.

W pre = pre-dialysis weight.

W post post-dialysis weight.

- The predialysis and postdialysis samples must be drawn at the same dialysis session.
- The predialysis urea blood sample was obtained from the arterial needle before administering any saline or heparin.
- The postdialysis urea blood sample was obtained at the end of the dialysis session by slowing the blood pump to 50-100 ml/min for 10-20 sec, after which the blood pump was stopped and a blood sample was obtained either from the arterial bloodline sampling port or from the

tubing attached to the arterial needle. The postdialysis urea blood sample must not be diluted by either recirculation or saline.

Statistical analysis of the data: Data were analyzed with statistical program "SPSS" under windows v. 6.21.

RESULTS

Our results are shown in Tables 1 to 15 and Figures 1 to 6. Table 1 shows the characteristic data of the studied group as regard age and gender. The etiology of chronic renal failure in the studied group was shown in Table 2 and Figure 1. The most common cause is unknown (36.3%), followed by chronic familial interstitial nephritis (13.3%) and focal segmental glomerulosclerosis (10%). Table 3 shows the laboratory parameters in the studied group. Duration of dialysis, hemodialysis session length, pump rate, dialyzer surface area and Kt/V in the studied group are presented in Tables 4. 5, 6, 7 and 8 respectively.

There was a significant positive correlation between Kt/V and pump rate, surface area of the dialyzer and duration of the dialysis as shown in Tables 9, 10 and 11. Table 12 shows highly significant positive correlation between Kt/V and dialysis session length. Also there was highly significant positive correlation between Kt/V and serum albumin as shown in Table 13 and Figure 2. No significant correlation was found between Kt/V and other laboratory parameters or blood pressure as presented in Tables 13 and 14 respectiv ely. The most effective parameter affecting the dialysis efficiency is the dialysis session length as shown in Table 15.

Table 1: The demographic data of the studied group.

	Cases ***N= 30***
Age (years):	
X ± SD	13.02 ± 3.58
Range	6 – 20
Gender:	
Male	12 (40%)
Female	18 (60%)

Table 2: The underlying etiology of chronic renal failure in the studied group.

Causes	*No.*	*%*
Unknown	11	36.3
Familial Mediterranean fever with 2ry renal amylidosis	1	3.3
Focal segmental glomerulo-sclerosis	3	10.0
Chronic familial interstitial nephritis	4	13.3
Steroid resistant nephritic syndrome	2	6.7
Membranoproliferative glomerulonephritis	1	3.3
Sickle cell nephropathy	1	3.3
Rapidly progressive glomerulonephritis	1	3.3
Obstructive uropathy	3	10.0
Juvenile nephronophthisis	1	3.3
Diffuse proliferative glomerulonephritis	1	3.3
Neurogenic bladder	1	3.3

Table 3: Showing laboratory parameters of the studied group.

	Cases (n = 30)	
	Mean ± SD	***Range***
Ferritin ng/mL	1188.5 ± 1073.3	105.4-5338
PTH Pg/mL	452.2 ± 344.5	17.1-1266
Iron mg/dL	98.7 ± 61.1	14.1-273
PTT second	43.0 ± 10.9	32.1-86.6
PT second	13.5 ± 1.4	11.6-18.8
Urea before dialysis mg/dL	134.3 ± 39.6	81-242
Urea after dialysis mg/dL	40.76 ± 13.9	15-70
Creatinine mg/dL	7.1 ± 1.6	2.5-9.9
PO_4 mg/dL	5.4 ± 1.6	2.8-9.5
Ca mg/dL	7.3 ± 1.1	6-10.8
Platelets count $x10^3$/cm	221.1 ± 64.7	115-346
HB g/dL	9.0 ± 1.2	6.6-11.5
Albumin g/dL	2.36 ± 0.5	2-4.2

Table 4: Showing duration of dialysis in the studied group.

Duration of dialysis	***Mean ± SD***	2.9 ± 2.5
	Range	1 month – 8 year

Table 5: Showing duration of dialysis session in the studied group.

Duration of dialysis session	***Mean ± SD***	3.55 ± 0.5
	Range	2-4 hours

Table 6: Showing pump rate in the studied group.

Pump rate	*No.*	*%*
180 ml/minute	6	20%
200 ml/minute	24	80%

Table 7: Showing surface areas of the dialyzer in the studied group.

Surface area of the dialyzer	*No.*	*%*
0.4 m^2	1	3.3
0.7 m^2	16	43.3
1.0 m^2	6	20
1.3 m^2	10	33.3
Surface area of the dialyzer	*Mean ± SD*	0.95 ± 0.285
	Range	0.4-1.3

Table 8: Showing Kt/V in the studied group.

Kt/V	*Mean ± SD*	*Range*	*Normal level*
	1.128 ± 0.32	0.457-1.837	1.2

Table 9: Showing correlation between Kt/V and the pump rate.

	r	*p*
Pump rate	0.38	< 0.05 (sig.)

Table 10: Showing correlation between Kt/V and the surface area of the dialyzer.

	r	*p*
Surface area of the dialyzer	0.38	< 0.05 (sig.)

Table 11: Showing correlation between Kt/V and the duration of the dialysis.

	r	*p*
Duration of the dialysis	0.43	< 0.05 (sig.)

Table 12: Showing correlation between Kt/V and duration of dialysis session.

	r	*p*
Duration of dialysis session	0.5	< 0.01 (HS)

Table 13: Showing correlation between Kt/V and other parameters.

	r	*p*
Ferritin	- 0.29	> 0.05 (NS)
PTH	0.09	> 0.05 (NS)
Iron	0.23	> 0.05 (NS)
PTT	0.15	> 0.05 (NS)
PT	0.17	> 0.05 (NS)
Creatinine	0.2	> 0.05 (NS)
PO_4	0.22	> 0.05 (NS)
Ca	0.13	> 0.05 (NS)
Platelets	0.21	> 0.05 (NS)
HB	0.12	> 0.05 (NS)
Albumin	0.47	< 0.01 (HS)

Table 14: Showing correlation between Kt/V and blood pressure.

	r	*p*
Blood pressure	0.54	> 0.05 (NS)

Table 15: Showing multiple regression analysis.

	B ± SE	*F*	*p*
Duration of dialysis session	- 0.001 ± 0.00084	3.44	< 0.01

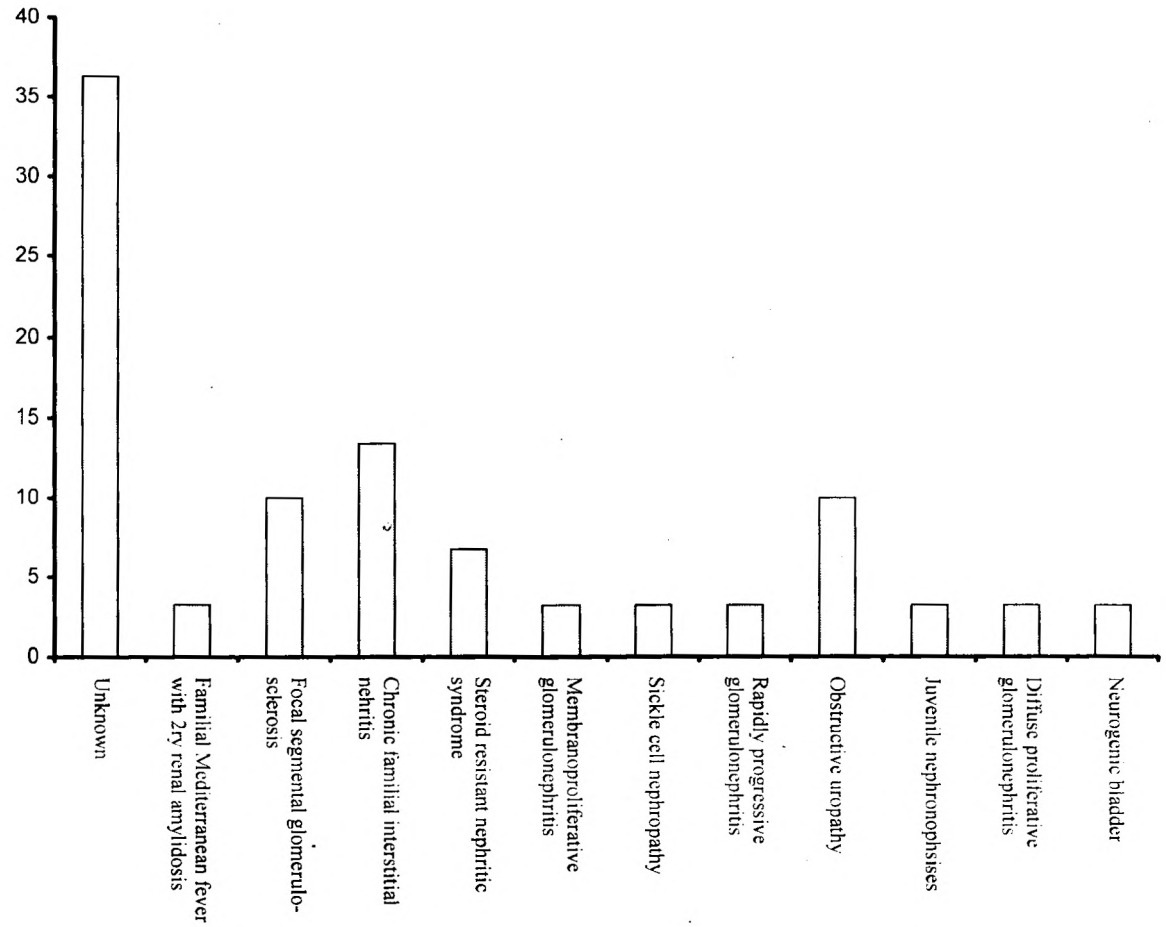

Fig. 1: The underlying etiology of chronic renal failure in the studied group.

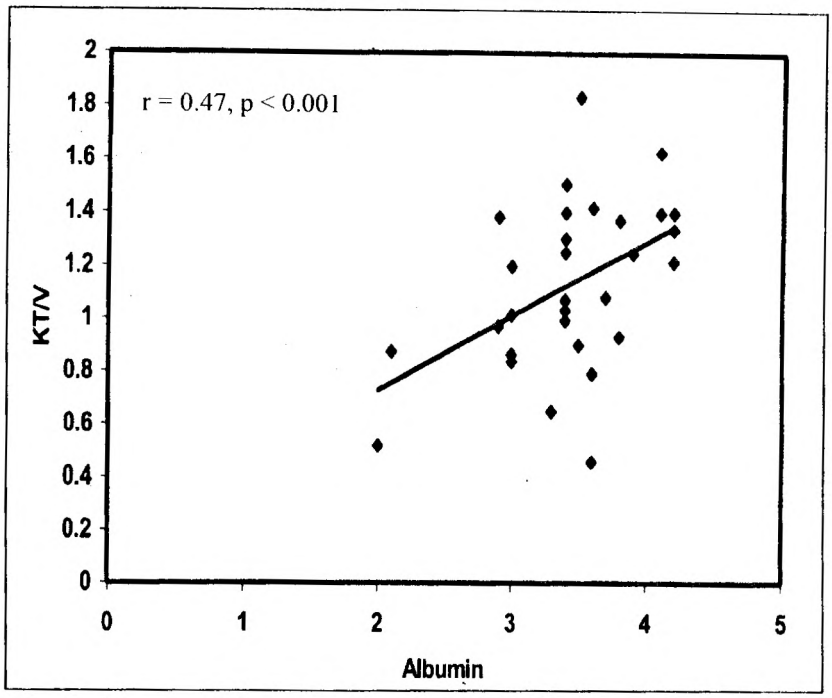

Fig. 2: Correlation between serum albumin and Kt/V.

DISCUSSION

Adequate hemodialysis can be defined as the amount of dialysis required for optimal patient survival[10]. Dialysis adequacy is. not easy to quantify. Clinically, several parameters must be considered to provide adequate dialysis, such as control of fluid overload and electrolytes disturbance, correction of metabolic acidosis and dialysis dose. The most commonly used parameter to evaluate delivered dialysis dose is the spKt/V index[2]. Without compromising the delivered dose of hemodialysis, efforts should be undertaken to modify the hemodialysis prescription to prevent the occurrence of intradialytic symptoms that adversely affect patient comfort and adherence(1 H. Measurement of the dialysis dose has, for the most part, relied on estimation of clearance of the small, water-soluble, nitrogenous waste product urea, and hence the mathematical model is referred to as urea kinetic modeling (UKM). It assumes that urea is distributed in a single, well-mixed pool. (Two-pool models exist but are generally considered not any more accurate to justify their complexity in daily use). UKM also assumes that urea is generated at a constant rate by protein metabolism and is removed at a constant rate by residual renal function, and intermittently by dialysis. IIence, in a person with negligible renal function, the extent of urea removal provides a measure of dialysis adequacy, and the rate of production correlates with dietary protein intake. Kt/V is a dimensionless ratio representing fractional urea clearance, 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). It is computed

using UKM. KUV derived from single-pool urea kinetics and is referred to as spKt/V. A value of spKt/V of 1 would imply that the total volume of blood completely cleared of urea during a dialysis session would be equal to the volume of distribution of urea. When dialysis flow rate and blood flow rate are increased, and the time on dialysis is shortened, the treatment is not as efficient because solute disequilibrium is enhanced and there is more time for solute to accumulate between dialysis sessions. Correction for the solute disequilibrium can be made by adjusting the Kt/V for the rebound in urea, which happens mainly in the 30-60 minutes immediately post dialysis. The resultant Kt/V is termed equilibrated KtN or eKtN. Another measure of delivered dialysis dose is the urea reduction ratio (URR)t[12] The reduction in urea as a result of dialysis, or the URR, is one measure of how effectively a dialysis treatment removed waste products from the bodv[13]. Although no fixed number can be said to represent an adequate dialysis, it has been shown that patients generally live longer and have fewer hospitalizations if the URR is at least 60 percent. For this reason, some groups advising on national standards have recommended a minimum URR of 65 percent([14]. The URR is usually meast'red only once every 12 to 14 treatmentst[5j]. The Kt/V is more accurate than the URR in measuring how much urea is removed during dialysis, primarily because the Kt/V also considers the amount of urea removed with excess fluid. Consider two patients with the same URR and the same post-dialysis weight, one with a weight loss of 1 Kg during the treatment and the other with a weight loss of 3 Kg. The patient who loses 3 Kg will have a higher Kt/V, even though both have the same URR 6),

According to NKF-KDOQI 2006 guidelines spKt/V > 1.2 or URR > 65% is recommended for maintenance, when a 3 times per week haemodialysis program is applied[17]. Another introduced approach estimates Kt/V from ionic "dialysance[10]. Advances in hemodialysis monitoring based an the conductivity monitoring (using sodium flux as a surrogate for urea) allow repeated and noninvasive measurement of delivered dialysis dose during each session. Because conductivity is related to ion concentration, it is possible to substitute one for the other in further calculations. The transfer characteristics of sodium and urea are similar, hence the ionic dialysance reflects the clearance of urea. The measurement of inlet and outlet dialysate conductivity enables software to measure ionic movement across the dialysis membrane. Kt/V can be calculated continuously without blood samples using ionic dialysance method. It is automatic, no need for blood draws, with no extra cost with regular dxalysis[G9]. In our study, we found significant positive correlation between pump flow rate and Kt/V and this may he explained by increase flow rate leads to increase filtration and removal of small molecular weight solutes. The above result was found also in the study done by I lassell et al., 2001 even in patients with low access flow, increasing dialyzer blood flow rate in general leads to an increase in delivered Kt/V regardless of vascular access flow rate[,°]. Also our result run with the studies done by Borzou et al., 2009 and Kim et al.,

2004 who confirmed that increa-sing the blood flow rate by 25% is effective in increasing dialysis adequacy and increasing blood flow rate by 15-20% of previous flow rate is effective in achieving dialysis adequacy in hemodialysis patients with low Kt/V respectively[1] "-). Our study showed significant positive correlation between duration of dialysis session and Kt/V and this may be explained by increased time of contact between blood and dialysate will remove a higher percentage of waste products. Patients with longer hemodialysis treatments have fewer complications secondary to ultrafiltration and thus are more likely to routinely achieve their estimated dry weight. As a result, they suffer fewer cardiovascular complications secondary to hypertension and/or hypervolemia. Saran. et al.. 2006 found the same result of longer dialysis session duration may be beneficial in several ways; improved tolerability of the treatment, greater removal of uremic toxins, particularly middle molecules, better control of blood pressure, and better volume management. These mechanisms may in turn reduce cardiovascular morbidity and mortaljty[23]. Longer treatment time is utilized in clinical practice as one of the methods to increase delivered KtIV which is confirmed by Marshall et al., 2006 who examine associations between HD dose and session length with mortality risk and support the inclusion of criteria relating to session length in definitions of adequate HD practice [24]. As all our patients attended 3 sessions per week, we could not assess the effect of frequency of dialysis on Kt/V but some studies showed improved Kt/V with increased frequency of dialysis. Zucchclli et al., 2005, found that daily HD leads to improve dialysis outcome. The basis for the beneficial effect is thought to be a more physiological clearance of solutes and water, with reduced pre-and post-I TI) solute concentration"[]. Chazot and Jean, 2009. found the positive effects of prolonged dialysis time or increased dialysis frequency lead to improvement of patients survival'2 [6]

As regards correlation between surface area of dialyzer and Kt/V we found positive correlation. This may be explained by increase filtration and removal of small molecular weight solutes from blood through membrane with more surface area. Azar, 2009, found that low flux and small surface area dialyzer did not show an improvement in Kt/V or URR with increase in dialysate flow rate[t2]" and another study done by Barth. 1996, showed that reducing treatment time will not affect the patient well-being if the dialyzer surface area inereased[(28)]. In our study, we found significant positive correlation between duration of dialysis and dialysis adequacy. It may be explained as the duration of dialysis prolonged the patient become more adapted and tolerated to dialysis regimen and dietary control that decrease urea production which is the same found by Rocco et al., 2001 [(29)]. We used in this study low flux dialyzer because it is the only available in our hemodialysis unit. The study done by Locatelli. Cavalli and Tucci, 2009, showed no significant difference between high-flux and low-flux membranes[(30)]. The effect of high-flux hemodialysis membranes on patient survival has not been unequivocally determined. However, the effect of high-

flux membrane showed a significant survival benefit in patients at risk for worse outcome, defined by serum albumin < 4 g/dl. Santoro A et al., 2008, showed high-flux dialyzer may improve survival independent of Kt/V[31]. A significant positive correlation between serum albumin and Kt/V was found in the present study. Our explanation for this positive correlation is that when adequate dialysis delivered to the patient anorexia is improved and the effect of uremia on GIT decreased. This leads to better appetite and decreased nausea and vomiting. This resulted in increase in protein intake and consequently increase in serum albumin level and vice versa. Several studies run in parallel to our result. Kalanter-Zadeh et al. 2003 found that normalized protein catabolic ratio (nPCR), reflects the daily protein intake in maintenance hemodialysis patients[32]. Several studies indicate that nPCR and Kt/V correlate with clinical outcome and also with each other. Thus, the relationship between low nPCR and poor outcome could be due to uremia, low Kt/V and this is in agreement with our explanation. Azar et al., 2007, suggested an association between improved survival and better nutritional status. Malnutrition is the main factor of morbidity and mortality among hemodialysis patients. It has been suggested that there is a correlation between dose of dialysis and nutritional status[33]. The National Cooperative Dialysis Study results show that protein catabolic rate and blood urea nitrogen (BUN) are important determinants of.morbidity in patients undergoing hemodialysis and also the serum albumin concentration as the most powerful indicator of mortality. Small decrease in serum albumin will cause a significant increase in mortality. Dose of dialysis and nutrition are considered to be interrelated. Marcus. Cohl and Uribarri, 1999, found the nutritional status is a strong predictor of outcome in hemodialysis patients. Adequate delivery of dialysis is necessary for hemodialysis patients to maintain their protein nutrition and provide evidence that protein intake in hemodialysis patients will increase with an increase in delivered dialysis above the level generally considered to be adequate[134].

REFERENCES

1. **Chiu, M.; Tse, K. and Lai, W. (2002):** Dialysis and Renal Transplantation in Children. Hk. J. Paediatr.; 7: 230-23.
2. **Francesco, Locatelli (2003):** Nephrol. Dial. Transplant.; 18: 1061-1065.
3. **Afshar; Jalali, Nadoushan; Sanavis and Komeilia (2006):** Assessment of hemodialysis adequacy in patient undergoing maintaince maneuver by laboratory tests. Iranian Journal of Pathology (UP) SPRING; 1(2): 55-60.
4. **Khalid, AI Saran; Alaa, Sabry; Mamdouh, Abdulghafour and Ahmed, Yehia (2009):** Online Conductivity, Monitoring of Dialysis Adequacy Versus Kt/V Derived from Urea reduction Ratio. International Journal of Nephrology and Renovascular Disease; 2: 27-31.
5. **Thomas, A.; Sacramento; John, T. Square; Goldstein, Houston; Victoria; Kumar, Klemens, B. Meyer; Keith, Norris and Lynwood (2006):** Clinical Practice Guidelines for Hemodialysis Adequacy, American journal of kidney disease; Pages S2-S90, Supplement I, Volume 48.
6. **Andrew, Kusiak; Bradley, Dixon and Shital, Shath (2004):** Predicting survival time for kidney dialysis patients. Computers in Biology and Medicine; 35: 311-327.
7. **V. Kovacic (2004):** Technical efficacy, Indian J. Nephrol.; 14: 1-9.
8. **Elaine, M. Spalding; Shahid, M. Chandna;**

Andrew, Davenport and Ken, Farrington (2008): Kt/V underestimates the hemodialysis dose in women and small men. Kidney Internationally; 348-355.

9. **Hand book of dialysis Oxford book (2005):** Page 240.
10. **Franssen, C. (2006):** Adenosine and dialysis hypotension. Kidney Int.; 69: 789-791.
11. Sorof, **J.; Brewer, E. and Portman, R. (2004):** Ambulatory blood pressure monitoring and interdialytic weight gain in children receiving chronic hemodialysis. Am. J. Kidney Dis.; 33: 667-674.
12. **Ankit, N.; Mehta; Andrew, Z. and Fenves (2010):** Hemodialysis. Adequacy Dialysis & Transplantation; January, Volume 39, Issue 1, pages 20-22.
13. Sarkar, J.; Agodoa, L.;,Jones, C. and Port, F. **(2006):** Body size, dose of hemodialysis, and mortality. Am. J. Kidney Dis.; 35: 80-88.
14. Casino, **M. and Lopez, L. (2000):** Prediction of creatinine clearance from serum creatinine. Nephron.; 16: 31-41, 1976.
15. Szczech, L.; Lowrie, **E.; Li, Z.; Lazarus, J.; Lew, N. and Owen, W. (2003):** Changing herodialysis thresholds for optimal survival. Kidney Int.; 59: 738-45.
16. **ANZ (Data Registry Report) (2006):** Australia and New Zealand Dialysis and Transplant Registry.
17. **Sofia, Zyga and Paul, Sarafis (2009):** Herodialysis adequacy. Health Science Journal; volume 3, issue 4.
18. **Jeroen, P.; Kooman; Frank, M.; vander Sande and Kare!, M. Leunissen (2010):** Kt/V; finding the tree within the woods. Oxford Journals, Nephrology Dialysis Transplantation; Volume 16, Issue 9, Pp. 1749-1752.
19. **Maria, Lourdes; Josefina, A.; Duenas; Antonio, V. and Cayco (2009):** Assessment of herodialysis adequacy ionic dialysance in comparison to standard method kt/v, Phil. J. Internal Medicine; 47: 19-23, Jan.-Feb.
20. **Hassell, D.; van der Sande, F.; Kooman, J.; Tordoir, J. and Leunissen, K. (2001):** Optimizing dialysis dose by increasing blood flow rate in patients with reduced vascular-access flow rate. Am. J. Kidney Dis.; Nov; 38 (5): 948-55.
21. 5. **Borzou; M.** Gholyaf; M. Zandiha; R. **Amini; M. Goodarzi and B. Torkaman (2009):** The effect of increasing blood flow rate on dialysis adequacy in hemodialysis patients, Saudi Journal of Kidney Diseases and Transplantation; Volume 20, Issue 4, Page 639-642.
22. **Kim, Y.; Song; Yoon; Shin and Chang (2004):** The effect of increasing blood flow rate on dialysis adequacy in hemodialysis patients with low Kt/V. Hemodialysis International; Volume 8, Issue I, page 85.
23. R. **Saran; J. Bragg-Gresham; N. Levin; Z. Twardowski; V. Wizemann; A. Saito; N. Kimata; B. Gillespie; C. Combe; J. Bommer; T. Akiba; D. Mapes; E. Young and F. Port (2006):** Longer treatment time and slower ultrafiltration in hemodialysis. International Society of Nephrology; 69, 1222-1228.
24. M. **Marshall; B.** Byrne; **P.** Kerr and S. **McDonald (2006):** Associations of hemodialysis dose and session length with mortality risk in Australian and New Zealand patients. Kidney International; 69, 1229-1236.
25. Piettro, **zucchelli; Umberto, Buoncritiani; Francesco, Locatelli; Bernard, Canaud and Hans, Kohler (2005):** Dialysis dose and frequency. Nephrol. Dial. Transplant.; 20-2: 285-296.
26. **Charles, Chazot and Guillaume, Jean (2009):** Effects of dialysis time and frequency on survival. Nature clinical practice nephrology, Vol 5 No 1. **Pregnanc** C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus **Precautions** Category D in third trimester of pregnancy; acute renal insufficiency, hyperkalemia, hyponatremia, interstitial nephritis, and renal papillary necrosis may occur; increases risk of acute renal failure in preexisting renal disease or compromised renal perfusion; low white blood cell counts occur rarely and usually return to the reference range in ongoing therapy; discontinuation of therapy may be necessary in persistent leukopenia, granulocytopenia, or thrombocytopenia; caution in patients with anticoagulation defects or patients who are receiving anticoagulant therapy.
27. Azar, **A. (2009):** Increasing dialysate flow rate increases diaiyzer urea clearance and dialysis efficiency: An in vivo study, Saudi Journal of Kidney Diseases and Transplantation. Volume 20, Issue 6, Page 1023-1029.
28. Robert, H. Barth (1996): High efficiency and high flux dialysis. Replacement of renal function by dialysis. Section 2, 418-453, DOI: 10.1007;' 978-0-585-36947-17.
29. Rocco, M.; Bedinger, NI.; Milam, **R.;** Greer, **J.; McClellan, W. and Frankenfield, D. (2001):** Duration of dialysis and its relationship to dialysis adequacy, anemia management, and serum albumin level. Am. J. Kidney Dis.: Oct: 38 (4): 813-23.
30. **Francesco, Locatelli; Andrea, Cavalli and Benedetta, Tucci (2009):** The growing problem of intradialytic hypertension. Nephrology Dialysis and Transplant; 8 (5): 325-329.
31. **Santoro, A.; Mancini, E.; Bolzani, R.; Boggi, R.; Cagnoli, L.; Francioso, A.; Fusaroli, M.; Piazza, V.; Rapana, R. and Strippoli, G. (2008):** The effect of on-line high-flux hemofiltration versus low-flux hemodialysis on mortality in chronic kidney failure. Am. J. Kidney Dis.; 52(3): 507-18.

32. **Kalanter-zadeh, K.; Supasyndh, O.; Lehn, R.; McAllister, C. and Koppie, J. (2003):** Normalized protein nitrogen appearance is correlated with hospitalization and mortality in hemodialysis patients with Kt]V greater than 1.2. J. Ref. Nutr. Jan., 13 (l): 15-25.

33. **Azar, A.; khaled, Wahb; Abdalla, Mohamed and Waleed, A. Massoud (2007):** Association between dialysis dose improvement and nutritional status among hemodialysis patients. American Journal of Nephrology. vol. 27. NO. 2.

34. **Marcus, R.; Cohl, E. and Uribarri, J. (1999):** Protein intake seems to respond to increase in KU V.