Research Article

Factors Affecting Decline of Residual Renal Function in Chronic Renal Failure Patients on Hemodialysis

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Abstract

Background: The importance of residual renal function (RRF) and its care has gained increased attention recently. It has been documented that preservation of residual renal function in dialysis patients improves quality of life as well as survival. The presence of residual renal function (RRF) in chronic dialysis patients contributes to improved clearance of uremic toxins while decline of RRF contributed significantly to anemia, inflammation, and malnutrition in end-stage renal disease (ESRD) patients. **Aim of the work**: is to compare different clinical and laboratory parameters among chronic renal failure patients on hemodialysis with lost RRF and with those with preserved RRF. **Methods:** A cross sectional observational study carried out at Minia University Hospital, Minia, Egypt. 100 patients with chronic renal failure recruited among the attendants of the dialysis unit from June 2013 to December 2013. Patients were divided into two groups, **group I** (n = 50) with lost RRF and **group II** (n=50) that have RRF defined by 24 hours urinary output of more than 200 ml per day, for both groups history, clinical examination and routine investigations, urine examination, parathyroid hormone, and echocardiography were done. **Results:** By doing logestic regression for both groups, it was found that female gender (OR= 1.4), presence of diabetes (OR=1.08), hypocalcemia (OR=7.67), hyperphosphatemia (OR=21) and hypo-albuminemia (OR=6.47) all are considered to be risk factors and predictors for loss of RRF in CRF patients on hemodialysis. **Conclusion:** Male gender, duration of dialysis per years, presence of diabetes, hypocalcemia, hyperphosphatemia and hypoalbuminemia all are considered to be risk factors and predictors of rapid loss of RRF in hemodialysis patients.

Keywords: Hemodialysis - Residual renal function - Chronic renal failure

Introduction

Chronic renal failure is a slow and progressive decline of kidney function. It's usually a result of a complication from another serious medical condition.

Residual renal function (RRF) is recognized as a significant factor influencing mor-bidity, mortality and quality of life in chronic dialysis patients[1]. In this condition patients need a replacement therapy in the form of peritoneal or hemodialysis so as to get rid of uremic toxins and its effect on different systems and improve quality of life in such patients[2].

The presence of residual renal function (RRF) in chronic dialysis patient's contri-butes to improved clearance of uremic toxins, in particular the clearance of middle molecules and protein-bound solutes[2]. Concentrations of uremic substances such as uric acid, B2 microglobulin are substantially lower in patients with RRF as compared with anuric patients. In addition, the need for dietary and fluid restriction is reduced, which may partly explain their better nutritional state and quality of life[3]. It has been shown that clinically important and statistically significant decreases in nutritional parameters occur with RRF loss. Furthermore, it has been demonstrated that small increments in RRF may account for major differences in quality of life[1].

In terms of clinical outcomes, the degree of RRF has been inversely associated with left ventricular hypertrophy [4].

Although RRF is often used to indicate remaining GFR, it also reflects remaining endocrine functions such as erythro-poietin production, calcium, phosphorus and vitamin D homeostasis, volume control, and removal of "middle molecules" or low molecular weight proteins[5].

The importance of identifying factors that protect and preserve RRF has been recognized among patients with chronic renal failure, pre-end-stage renal disease (ESRD). Control of BP, angiotensin-converting enzyme (ACE) inhibitors, decreasing proteinuria, dietary modify-cation, avoidance of nephrotoxins, and glucose control have all been considered integral parts of the pre-ESRD care[6]. Cause of ESRD, level of BP, and various medications have all been implicated as having an effect on RRF[7].

For HD patients, there has been debate in the literature about whether the type of dialyzer membrane has an effect on RRF. Some have suggested that biocompatible membranes preserve RRF for a longer time period [8].

RRF is clinically important in that it can account for major differences in dialysis requirements, since it contributes to measures of adequacy, both Kt/V urea and creatinine clearance (*C*Cr)[4].

However, these studies have methodo-logical limitations, including small sample size with inadequate statistical power, retrospective design, and lack of inclusion of all known predictor variables and other modifying factors. Few studies have comprehensively evaluated whether these or other factors are important in preserving RRF after initiation of dialysis.

Patients and Methods

This study included 100 chronic renal failure patients on maintenance hemo-dialysis, taken from dialysis unit, internal medicine department, Minia university Hospital, in the period from June 2013 to December 2013. Informed consent was taken from all patients and after approval of the medical ethical committee of the faculty of medicine, Minia University. Patients were subdivided into two groups. **Group I:** included 50 patients; they all are CRF patients on hemodialysis with lost residual renal function defined as urinary output less than 200ml/day. **Group II:** included 50 CRF patients with preserved RRF defined as urinary output 200ml / day or more.

Inclusion criteria: Chronic renal failure, on maintenance hemodialysis from at least 6 months. **Exclusion criteria**: Obstructive uropathy, Heart failure, Chronic liver disease (decompensated liver cirrhosis and ascites), Acute renal failure, Dehydration, Uncontrolled diabetes mellitus, use of contrasts and NSAIDs

All patients were subjected to the following: A- Full clinical assessment; including: Medical history Age, Sex, Duration of dialysis, Cause of renal failure, Compliance on dialysis, history of diabetes or hypertension, Concomitant chronic illness, Response to erythropoietin stimu-lating agents, Compliance to phosphate lowering agents.

Clinical parameters (Pre and post dialysis blood pressure, Dry weight, Dialysis treatment parameters (frequ-ency, session length, intradialytic weight loss [pre-post weight], and type of vascular access), Adequacy of dialysis is determined by using Kt / V formula which was calculated online using pre and post dialysis blood urea nitrogen, Prescribed medication (phosphate- binding agents, erythropoietin stimulating agents (ESAs).

B- Laboratory investigations, in the form of: 1- Complete blood count, Serum calcium and phosphate level, Lipid profile, Complete liver function tests, B2 micro-globulin level, Parathormone hormone level, Uric acid level, Urine analysis.

A- **Blood samples**: 10ml venous blood were generally drawn on the first session of the week before dialysis, for routine laboratory assessments: Two ml of venous blood on EDTA containing tube for CBC, RBCs indices, platelet count and differential WBCs count using Minidry 3200 auto cell counter. Another two ml for serum albumin determined by spectro-

photometer. Three ml of venous blood on a plain plastic tube left to be clotted in the incubator and centrifuged to be separated for assessment of the serum calcium, phosphorus, uric acid, renal functions. Using Dimension ES chemical auto-analyzer. Serum B2-Microglobulin: using ELISA kits supplied from ORGENTEC Diagnostika company in which cut off value equal to 3 microgram per ml. Lipogram: Serum cholesterol and triglycerides drawn after fasting for about 12 hours, the cut off value for cholesterol is 200 mg / ml and for triglycerides is 150 mg/ml. An additional blood sample was drawn after dialysis for determination of post dialysis urea and creatinine concentration done on Dimension ES chemical auto-analyzer. Parathormone hormone level: using ELISA based kits supplied from DIA source Immuno Assays S.A., in which cut off point equal to 55 picogram per ml.

2- **Urine assessment**: In the form of simple urine analysis to detect albuminuria

Results

The study included 100 patients with chronic renal failure on hemodialysis divided into two groups, Group I, anuric chronic renal failure patients on hemo-dialysis consists of 50 patients 33 males (66%) and 17 females (34%), their mean age 52.54±18.34, and Group II which consisted of 50 patients have residual renal function 29 male (58%) and 21 female (42%), their mean age 47.3± 16.05. (demographic data summarized in table 1). By doing logestic regression for both groups, it was found that female gender (OR= 1.4), presence of diabetes (OR = 1.08), hypocalcemia (OR=7.67), hyper-phosphatemia (OR=21) and hypo-albuminemia (OR=6.47) all are considered to be a risk factors and predictors for loss of RRF in CRF patients on hemodialysis (table 2).

3- **Radiological assessment**:

A- Echocardiography: The echocardiogram was performed with the patient breathing quietly and lying in the left lateral position. Four acoustic views (parasternal long axis, parasternal short axis, apical four chambers, and apical two chambers) were obtained. Left ventricular hypertrophy detected by measuring the end diastolic diameter of left ventricle (IVSD) using M-mode recording under guidance of 2D Echocardiography according to the recommendation of the American Society of Echocardiography (LVH is evident when IVSD more than 1mm).

B- Abdominal sonar: With special interest in kidneys size, echogenicity and position.

Statistical analysis

Data were analyzed using Statistical Package for the Social Science (SPSS for windows version 20.0). The continuous variables were expressed as mean ± SD which compared using chi-square test. Statistical significance was defined as a probability level of $P \leq 0.05$.

Table (1): Show the demographic data of the two studied group:

Demographic data	Group I Anuric (n = 50)	Group II RRF (n = 50)	P value
Age: M ± SD	52.54 ± 18.34	47.3 ± 16.05	0.132
Sex: Male. Female.	33 (66%) 17 (34%)	29 (58%) 21 (42%)	0.410

Table (2): Documented risk factors (PREDICTORS) for loss of residual renal function in the studied patients:

Variable	Group I (anuric)	Group II (RRF)	P value	OR (95% CI)	P value
Age:	52.54 ± 18.35	47.3 ± 16.06	0.132	0.98 (0.96-1.01)	0.132
Duration of dialysis	7.31 ± 3.95	7.58 ± 2.35	0.677	1.03 (0.91-1.16)	0.674
Sex: **Male.** **Female.**	 33 (66%) 17 (34%)	 29 (58%) 21 (42%)	0.410	 1.41(0.62-3.16) 0.71(0.32-1.6)	 0.411 0.411
DM: **Yes.** **No.**	 10 (20%) 40 (80%)	 5 (10%) 45 (90%)	0.042	1.08 (0.11-1.09)	0.040
Calcium: **<8.** **>8.**	 23 (46%) 27 (54%)	 5 (10%) 45 (50%)	<0.001*	7.67 (2.61-22.54)	<0.001*
Phosphorous: **>7.** **<7.**	 15 (30%) 35 (70%)	 1 (2%) 49 (98%)	<0.001*	21 (2.65-166.46)	0.004*
Albumin: **<3.5.** **>3.5.**	 18 (36%) 32 (64%)	 4 (8%) 46 (92%)	0.001*	6.47 (2-20.92)	0.002*

Table (3) shows that the duration of dialysis was higher in group 1 (7.58 ±2.34) than in group 2 (7.30±3.95) with no significant difference (p=0.677), more ever the effect of dialysis as measured by kt/ v was higher in group 2 (3.1±0.75) than in group 1 (0.87±0.17) with significant difference ($p \leq 0.005$), and finally intra dialytic weight loss was more in group 1 than in group 2 which is statistically significant ($p \leq 0.001$). As measured by number of ampules per weak which was higher in group I (3.13± 1.2) than group II (2.21±1.15), ($p \leq 0.001$), also it shows the relation between number of ampules and hemoglobin percent which was strongly correlated in group II (r=0.867) and weekly correlated in group I (r=0.187) (Table (4).

Table (5): represent the prevalence of left ventricular hypertrophy in both groups measured by intra ventricular septum diameter in diastole measured by mm which was more in group I (2.44±1.25) than group II (1.1±0.58), another effect is the presence of hypertension which was more in group I than group II for systolic blood pressure (149 ± 23.66 vs. 128.5± 21.5, p<0.001) and for diastolic (86±18.73 vs. 78±13.85, p<0.017).

Serum cholesterol was higher in group I than group II (240.68± 64.83 vs. 166.71± 48.2), also triglycerides was higher in group I than group II (155.82±49.97 vs. 105.66 ±38.03) with p< 0.001 for all as shown in Table (6).

AS regards the prevalence and duration of hypertension in both groups: in group I, 41 patients (82%) have hypertension and 9 patient (18%) don't have the disease, in group II, 37 patients (74%) had hypertension and 13(26%) don't have the disease which was weekly significant, while duration was higher in group I (10.71±7.28 years) than in group II (6.47±5.61 years) which was significant (p= 0.005).

The prevalence and duration of diabetes in both groups: it was 5(10%) have the disease in group I while 45(90%) don't have the disease, while in group II, 12 have the disease (24%) while 38(76%) don't have the disease, which was weekly significant, the duration was higher in group I (19.6±1.51

years) than in group II (11.16 ± 7.48 years) which was significant (p = 0.004).

As regards the percentage of patients taking phosphate lowering agents (PH.L.A) in both groups: Which was as following: in group I, 42 patients were taking these agents (84%) while 8 (16%) don't take these agents, in group II, 40 (80%) patients were taking these drugs while 10(20%) patients don't and the difference was not significant (p=0.603).

Biochemical parameters in the studied groups was shown in Table (7). It shows that albumin level was higher in group II (4.17±0.57) than group I (3. 64±0.53), phosphate(PH) level was higher in group I (6.65±0.83) than in group II (5.81± 0.50), calcium (Ca) level was higher in group II (8.41±0.49) than in group I (7.83 ± 0.62), while uric acid level was higher in group I (5.51± 1.16) than in group II (3.49 ± 0.79), the difference for whole above results were statistically significant (p≤0.001).

Table (3): Dialysis characteristics

Dialysis Characteristics	Group I (Anuric) N = (50)	Group II (RRF) N = 50	P value
Duration of Dialysis (years) M ± SD	7.30 ± 3.95	7.58 ± 2.34	0.677
Kt/v M ± SD	0.87 ± 0.17	3.1 ± 0.75	<0.001*
Intra-dialysis wt. loss (kg) M ± SD	3.12 ± 1.46	2.05 ± 1.54	<0.001*

Table (4): shows the response to erythropoietin stimulating agents (ESA)

	Group I (Anuric) (n = 46)		**Group II** (RRF) (n = 46)		**P value**
ESA dose ampules per week M ± SD	3.13 ± 1.2		2.21 ± 1.15		< 0.001*
ESA dose and Hb	**r**	**p**	**r**	**P**	
	0.187	0.213	0.867	<0.001*	

Table (5): Cardiovascular changes in both groups

	Group I Anuric (n = 50)	**Group II RRF** (n = 50)	P value
LVH (IVSD) By mm M ± SD	2.44 ± 1.25	1.1 ± 0.58	< 0.001*
Systolic Bl.p: mmHg M ± SD	149.16 ± 23.66	128.5 ± 21.52	< 0.001*
Diastolic Bl.p: mmHg M ± SD	86 ± 18.73	78 ± 13.85	0.017*

Table (6): Lipid profile in the studied groups

Lipid profile	**Group I Anuric** (n = 50)	**Group II RRF** (n = 50)	P value
TC: mg % M ± SD	240.46 ± 64.83	166.71 ± 48.2	< 0.001*
TG: mg% M ± SD	155.82 ± 49.97	105.66 ± 38.03	< 0.001*

Table (7): Some biochemical parameters in the studied groups

	Group I **Anuric** (n = 50)	Group II **RRF** (n = 50)	P value
Albumin: mg% M ± SD	3.64 ± 0.53	4.17 ± 0.57	< 0.001*
PH: mg/dl M ± SD	6.65 ± 0.83	5.81 ± 0.50	< 0.001*
Ca: mg/dl M ± SD	7.83 ± 0.62	8.41 ± 0.49	< 0.001*
Uric acid: mg/dl M ± SD	5.51 ± 1.16	3.74 ± 0.79	< 0.001*

Tables 8 and 9: compare the level of both calcium and phosphorus in those taking phosphate lowering agents and those don't in both studied groups as follow: In group I: Calcium level is higher in patients taking these agents (8.01 ± 0.48) than in those who don't take (6. 81± 0.88), while phosphorus level is lower in those taking these agents (6.43 ± 0.62) than in those don't take (7. 81 ± 0.88), the difference are highly significant with p<0.001 for all. **In group II :** calcium level was higher in patients taking these agents (8.59 ± 0.24) than in those who don't take (7. 68 ± 0.60), while phosphorus level was lower in those taking these agents (5.6 ± 0.27) than in those who don't take (6. 63 ± 0.35), these results were highly significant with p< 0.001 for all.**Table (8)**: Levels of Calcium and phosphorous in those taking PH.L.A. agents and those who don't take in group I

Group I Anuric	**With PH.L.A**. (n =42)	**Without PH.L.A** (n = 8)	P value
Ca:M ± SD	8.01 ± 0.48	6.87 ± 0.35	< 0.001*
PH: M ± SD	6.43 ± 0.62	7.81 ± 0.88	< 0.001*

Table (9): Levels of Calcium and phosphorous in those taking PH.L.A. agents and those who don't take in group II

Group II RRF	**With PH.L.A**. (n =40)	**Without PH.L.A** (n = 10)	P value
Ca: M ± SD	8.59 ± 0.24	7.68 ± 0.60	0.001*
PH: M ± SD	5.6 ± 0.27	6.63 ± 0.33	< 0.001*

Table (10), figure (1): shows the level of beta 2 microglobulin (B2MG): which was higher in group I (3.79 ± 0.94) than in group II (1.82 ± 1.02), and the difference was highly significant (p = 0.001).

	Group I **Anuric** (n=50)	Group II **RRF** (n=50)	P value
B2 MG Microgram /dl M ± SD	3.79 ± 0.94	1.81 ± 1.02	< 0.001*

Table (10): The level of beta 2 microglobulin (B2MG) in patients

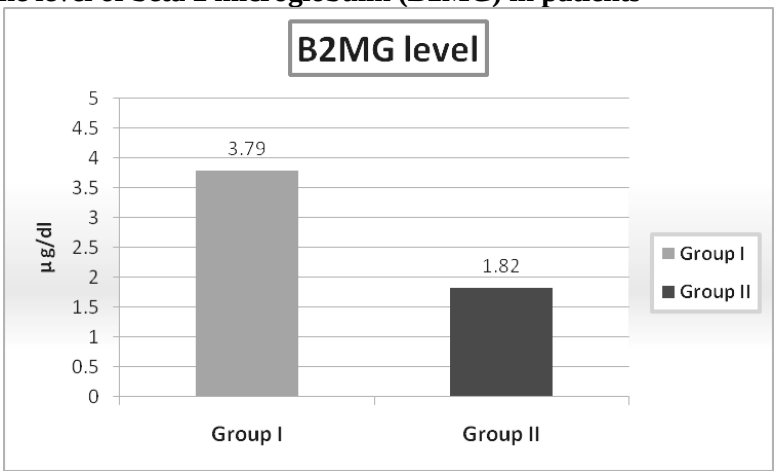

Fig. (1): Level of B2- microglubulin level in the studied groups

The level of parathormone hormone **(PTH) level** was higher in group I (51. 16 ± 9.3) than in group II (31.58± 9.50), and the difference between the two groups is highly significant (p = 0.001).

Table (11): Level of parathormone hormone in the studied groups

	Group I Anuric (n=50)	**Group II** RRF (n=50)	P value
PTH Pg/dl M ± SD	51.16± 9.3	31.58 ± 9.50	≤ 0.001

Discussion

The maintenance of residual renal function must be a primary objective in patients starting treatment with haemodialysis, since this provides major benefits in terms of patient survival [9].

The gradual deterioration of RRF in patients with end-stage renal disease starting dialytic therapy depends not on a single mechanism but rather on a number of factors operating simultaneously [5].

A higher dialysis dose cannot compensate for declining RRF[10]. The increased benefit of RRF compared to dialysis clearance is likely attributable to a better water and salt balance, the renal ability to clear and metabolize various substances including middle-sized molecules such as β-2-microglobulin and protein-bound substances[11] as well as the endocrine functions of the kidneys.

Decline of RRF also contributed signifycantly to anemia, inflammation[12], and malnutrition in end-stage renal disease (ESRD) patients[3]. More importantly, RRF has also been shown to be a powerful predictor of mortality, especially in patients on hemodialysis (HD)[13].

On studying the level of hemoglobin and the response to ESA in patients with RRF and those with lost RRF in our study. We found a higher hemoglobin level (11.71± 1.07) in group II versus (9.93±1.58) in group I and increased response to ESA in patients with preserved RRF than in those with lost RRF respectively, and the results were significant (p≤001), also the correlation between dose of ESA and hemoglobin level was strong positive in patients with preserved RRF (r = 0.867), and weakly positive in patients with lost RRF (r= 0.187).

On studying the serum phosphate level in both studied groups we found that serum phosphate level was higher in those with lost RRF (6.65 ± 0.83) than in those with preserved RRF (5.81± 0.50), (p≤0.001). In a rat model, low-phosphate diets showed protection of RRF regardless of dietary protein content[14]. This is supported by a study in humans demonstrating that a high

phosphate level was a risk factor for RRF decline and mortality in pre-dialysis patients[15].

In contrast to serum calcium which was lower in patients with hyperphosphatemia in patients with lost RRF. Our results were in agreement with Penne et al., 2011[16], in which phosphate level in those with lost RRF (5.1±1.62) was higher than those with preserved RRF (4.77±1.17), p=0.008 in his study which was conducted on 552 patients.

The difference between percentage of patients taking phosphate lowering agents and those who did not take was not significant (p=0.603). No randomized trials in humans have elucidated if low phosphate blood levels can protect RRF or which phosphate binder to use.

On studying the serum albumin level we found that serum albumin was higher in patients with preserved RRF, than in those with lost RRF and this difference was significant (p= 0.001). This was noted by Penne et al.,[16] who reported that there was a difference between the two groups as regard serum albumin, although this was not significant (p= 0.26) and this was linked to increased resistance to ESA in patients with lost RRF due to the fact that low albumin is indicative to low available iron for erythropoiesis[17]. Also this observation was also noted by Takeshi et al.,[18] who reported higher level of albumin in patients with preserved RRF, (p=0.03), and this was explained by better nutritional status in patients with preserved RRF.

On studying the serum level of B2 microglobulin, it was noted that it was higher in patients with lost RRF than in those with preserved RRF, and this was highly significant (p = 0.001). This was in agreement with *Penne* et al.,[16], who reported a significant difference in his results between both patient subsets which was conducted on 552 patients (p = 0.001). This reflect the role of RRF in elimination and removal of B2 microglobulin which is responsible for many musculoskeletal manifestations in CRF patients[19]. Residual kidney function and dialyzer clearance, the duration of ESRD and body composition were independent determinants of serum B-2M levels in chronic hemodialysis patients. The mean predialysis serum B-2M level over time was predictive of all-cause mortality, independent of the chronicity of dialysis and residual kidney function[20]. The presence of residual renal function (RRF) in chronic dialysis patients contributes to improved clearance of uremic toxins, in particular the clearance of middle molecules and protein-bound solutes [3].

On studying the level of parathormone hormone in blood we found a higher level of this hormone in patients with lost RRF than in patients with preserved RRF (p = 0.001). This is mostly due to hyperphosphatemia which leads to secondary hyperparathyroidism. This observation was in agreement with Penne et al, [16], and with Takeshi et al., [18].

In our study we found that hypertension and left ventricular hypertrophy are more prevalent in patients with lost RRF than in patients with preserved RRF and this difference was significant (p= 0.001). This was in agreement with Menon et al., [21] and Ates et al.,[22] who reported that preservation of RRF is associated with normotension, euvolemia and more normal left ventricular mass index.

Maintaining good blood pressure control should also serve as an important measure in preserving residual renal function in dialysis patients. This indicates the importance to avoid over-zealous ultra-filtration and intra-dialytic hypotension while trying to achieve fluid balance in dialysis patients, as this may have detrimental effects on residual renal function[7,23].

In our study hypercholestrolemia and hypertriglyceridemia are more prevalent in patients with lost RRF than in those with preserved RRF and the difference was highly significant (P= 0.001) and this was in agreement with YU-FENG LIN et al.,[24] who reported significant difference between the two groups (p= 0.03).

On studying the predictors for loss of residual renal function in studied patients

we found that male gender was a predictor for more rapid loss of residual renal function than female gender (OR=1.4), this was in agreement with Data from the MDRD study which had indicated a slower mean GFR decline in women compared to men with chronic renal failure. However, gender differences were reduced and no longer significant after controlling for base-line proteinuria, MAP, HDL cholesterol[25].

On studying other parameters, we found that duration on dialysis per years was not strongly significant as a predictor for loss of RRF. Another important parameter is the presence of diabetes which is considered an important risk factor for rapid loss of RRF (OR= 1.08), this was consistent with Moist et al.,[5] who also considered diabetes as an important risk factor for rapid loss of RRF.

Low level of serum calcium was estimated to be a strong predictor for rapid loss of RRF in our study (OR=7.6), this was also in agreement with Moist et al.,[5] who suggest that this observation may be due to the concurrent hyperphosphatemia that lead to more rapid loss of RRF.

Sung et al.,[26] reported that generation of inflammatory mediators during the process of hemodialysis especially with low flux membrane lead to more rapid loss of RRF, of which hypoalbuminemia is considered one of these inflammatory mediators and low albumin level is considered a risk factors for loss of RRF (OR= 6.47) and this was also in agreement with Perl & Bargman study[27].

Conclusions:

Male gender, duration of dialysis per years, presence of diabetes, hypocalcemia and hypoalbuminemia all are considered to be risk factors and predictors of rapid loss of RRF in hemodialysis patients

Recommendation:

Higher doses of ESA should be used in patients with lost RRF to compensate for the lost endocrine function of the kidney by improving level of hemoglobin. Also higher doses of phosphate lowering agents should be used in these patients to improve phosphate level, calcium level and reduce incidence of secondary hyperparathyroi-dism. Use of high flux filters is desired. Moreover, screening for cardiovascular diseases and control of hyperlipidemia should be done also in anuric CRF patients to reduce the risk of cardiovascular diseases.

References

1- Merkus MP, Jager KJ & Dekker FW et al. Predictors of poor outcome in chronic dialysis patients: The Nether-lands Coope-rative Study on the Adequacy of Dialysis. The NECOSAD Study Group. Am J Kidney Dis 2000; 35:69−79

2- Wang AY, Lai KN. The importance of residual renal function in dialysis patients. Kidney Int. 2006 May; 69 (10):1726-32.

3- Wang AY, Woo J, Wang M, Sea MM, Sanderson JE, Lui SF, Li PK: Important differentiation of factors that predict outcome in HEMO dialysis patients with different degrees of residual renal function. Nephrol Dial Transplant 2011; 20:396–403.

4- Bargman JM, Golper TA: The importance of residual renal function for patients on dialysis. Nephrol Dial Transplant 2005; 20:671–673.

5- Moist LM, Port FK, Orzol SM, Young EW, Ostbye T, Wolfe RA, et al. Predictors of loss of residual renal function among new dialysis patients. J Am Soc Nephrol 2000;11:556–64.

6- Li PK, Chow KM, Wong TY, Leung CB & Szeto CC. Effects of an angiot-ensine converting enzyme inhibitor on residual renal function in patients receiving HEMO dialysis. A randomized, contro-lled study. Ann Intern Med 2010; Vol.139, No.2, pp.105-112.

7- Jansen MA, Hart AA, Korevaar JC, Dekker FW, Boeschoten EW, Krediet RT on behalf of the NECOSAD Study Group. Predictors of the rate of decline of residual renal function in incident dialysis patients. Kidney Int 2010; 62: 1046–53.

8- Hartmann J, Fricke H, Schittle H: Biocompatible membranes preserve renal function in patients undergoing hemodialysis. Am J Kidney Dis 1997;30:366-373

9- Lucas M, Briones J, Couto A, Pérez J. Maintaining residual renal function in patients on haemodialysis: 5-year experi-

ence using a progressively increasing dialysis regimen. Nefrologia 2012; 32(6): 767-76.

10- Vilar E, Wellsted D, Chandna SM, et al. Residual renal function improves outcome in incremental haemodialysis despite reduced dialysis dose. Nephrol Dial Transplant 2009;24:2502-2510.

11- Bargman JM, Thorpe KE, Churchill DN: Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. J Am Soc Nephrol 2010; 12:2158– 2162.

12- Cobo G, Qureshi AR, Lindholm B, Stenvinkel P. C-reactive Protein: Repeated Measurements will Imp-rove Dialysis Patient Care. Seminars in dialysis, 2015, 1525-1539

13- Thijssen S, Kotanko P, Kuhlmann MK, Bergman M, Winchester JF, Levin NW. The impact of residual renal function on hospitalization and mortality in incident hemodialysis patients. Blood Purif 2011; Vol.31, No. 4, pp. 243-251.

14- Kusano K, Segawa H, Ohnishi R, et al. Role of low protein and low phosphorus diet in the progression of chronic kidney disease in uremic rats. J Nutr Sci Vitaminol (Tokyo) 2008;54: 237-243.

15- Voormolen N, Noordzij M Grootendorst DC, et al. High plasma phosphate as a risk factor for decline in renal function and mortality in predialysis patients. Nephrol Dial Transplant 2007; 22:2909-2916

16- Penne EL, van der Weerd NC, Grooteman MP, Mazairac AH, van den Dorpel MA, Nube MJ, Bots ML, Levesque R, ter Wee PM, Blankestijn PJ: Role of residual renal function in phosphate control and anemia management in chronic hemodialysis patients. Clin J Am Soc Nephrol 2011; 6:281–289.

17- Agarwal R, Davis JL, Smith L: Serum albumin is strongly associated with erythropoietin sensitivity in hemodialysis patients. Clin J Am Soc Nephrol *2008;* 3: 98–104.

18- Takeshi Suda, Kinya Hiroshige, Takayuki Ohta, Yujiro Watanabe, Masako Iwamoto, Kaori Kanegae, Akira Ohtani and Yasuhide Naka-shima. The contribution of residual renal function to overall nutritional status in chronic haemodialysis patients. Nephrol. Dial. Transplant. (2009)15 (3): 396-401.

19- Shea PH, Maher JF, Horak E: Prediction of glomerular filtration rate by serum creatinine and B2 micro globulin. Nephron 2011; 29: 3035.

20- Cheung AK, Rocco MV, Yan G, Leypoldt JK, Levin NW, Greene T, Agodoa L, Bailey J. Serum B-2 Microglobulin Levels Predict Morta-lity in Dialysis Patients: Results of the HEMO Study. J Am Soc Nephrol 2006; 17: 546–555.

21- Menon MK, Naimark DM, Bargman JM, Vas SI, Oreopoulos DG: Longterm blood pressure control in a cohort of peritoneal dialysis patients and its association with residual renal function. Nephrol Dial Transplant 2011;16:2207–2213.

22- Ates K, Nergizoglu G, Keven K, Sen A, Kutlay S, Ertürk S, Duman N, Karatan O & Ertuğ AE. Effect of fluid and sodium removal on mortality in peritoneal dialysis patients. *Kidney Int* 2012Vol.60, No.2, pp.767-776.

23- Lazarus JM, Owen WF. Role of bio incompatibility in dialysis morbidity and mortality. Am J Kidney Dis 2012;24: 10191032.

24- Yu-Feng Lin, Jeng-Wen Huang, Ming-Shiou Wu, Tzong-Shinn Chu, Shuei-Liong Lin, Yung-Ming Chen, Tun-Jun Tsai, Kwan-Dun Wu. Comparison of residual renal function in patients undergoing twice-weekly versus three times weekly haemodialysis. Nephrology 2009 Feb 19;14(1):59-64

25- Hunsicker LG, Adler S, Cagsiulla A, England B, Greene T, Kusek JW, Rogers NL, Teschen PE: Predictors of progression of renal disease in the Modification of Diet in Renal Disease Study. Kidney Int. 1997;51,1908-1919.

26- Sung Hee Chung, Olof Heimbürger, Peter Stenvinkel, Jonas Bergström, and Bengt Lindholm. Association between inflammation and changes in residual renal function and peritoneal transport rate during the first year of dialysis.

27- Nephrol. Dial. Transplant. 2001;16 (11): 2240-2245

28- Perl J, Bargman JM. The importance of residual kidney function for patients on dialysis: a critical review. Am J Kidney Dis 2009; 53:1068-1081