Impacts of residual renal function (RRF) on clinical and laboratory features of chronic hemodialysis patients

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Abstract: Objective: To study the effect of residual renal function (RRF) on clinical and laboratory features of chronic haemodialysis patients. **Background:** Residual renal function (RRF) in patients with end-stage renal disease (ESRD) is defined as the ability of native kidneys to eliminate water and uremic toxins. Studying the impacts on haemodialysis patients will guide nephrologist for better preservation of (RRF) and so improve outcome of their patients. **Patients and Methods:** The clinical and laboratory data of 73 regular haemodialysis patients(more than 3 months) of dialysis unit at our Department of Internal Medicine and during a 6 month period from October 2016 to March 2017 were reviewed in a retrospective manner the patients classified according to presence of (RRF) and not to two groups. **Results:** this study reveal that hypertension is the main cause of renal failure in both groups and show significant correlation between(RRF)(positive for group having residual function) and ultrafiltration rate, serum creatinine, serum potassium, haemoglobin level, serum iron, transferrin saturation, intact parathyroid hormone and CRP and no correlation between (RRF) and blood pressure, heart rate, body mass index, serum urea, serum sodium, calcium, phosphorus, uric acid, serum ferritin and serum albumin. **Conclusion:** residual renal function has clinical and laboratory effects on our patients of residual and provide them better survival than patients of non residual. Our study about (RRF) on dialysis patients confirms most of the findings of previous studies that clarify the importance of (RRF) on patients' survival and the importance of its preservation.

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1. Introduction

Residual renal function (RRF) in patients with end-stage renal disease (ESRD) receiving renal replacement therapy is defined as the ability of native kidneys to eliminate water and uremic toxins. In clinical practice, it is considered synonymous with such parameters as daily diuresis and/or glomerular filtration rate (GFR). The optimal method to measure RRF has not been established**.[1]**

Residual renal function (RRF) remains important even after beginning of dialysis. RRF contributes significantly to the overall health and well-being of patients on dialysis.**[2]**

Much of RRF is lost during the first 18 months of hemodialysis, and appears to depend on the primary cause (s) of kidney failure as well as other patient- and treatment-related factors.**[3]**

It plays an important role in maintaining fluid balance, phosphorus control, nutrition, and removal of middle molecular uremic toxins and shows inverse relationships with valvular calcification and cardiac hypertrophy in patients on dialysis. Decline of residual renal function also contributes significantly to anemia, inflammation, and malnutrition in patients on dialysis.**[4]** It is not surprising to find that residual renal function also contributes significantly to the quality of life of dialysis patients. The clinicians should be aware of clinical importance of RRF in the management of other patients.**[5]**

RRF may allow for a reduction in the duration of hemodialysis sessions and the need for dietary and fluid restrictions in both patients on peritoneal dialysis and hemodialysis. More importantly, the loss of RRF is a powerful predictor of mortality.**[2]**

2. Patients and methods

This study will be carried out on seventy three of subjects on regular haemodialysis sessions in haemodialysis unit of Internal Medicine Department and ELmanshia unit at Menoufia University. All will be given informed consent and the study will be approved by the ethics committee of Menoufia University.

Criteria of selection: patients on regular HD for more than 3 months more than18 years old and exclude Patient on diuretics**,** Pregnancy, Malignancy and Infection.

The subjects were divided into two groups**. Group (1):** 24 patients with preserved residual renal

function. **Group (2):**49 patients don't have preserved residual renal function.

All participants will be subjected to ***detailed medical history (*** Age(years), Duration of dialysis (months), Cause of ESRD, History of hypertension, History of diabetes, History of ischemic heart disease and History of heart failure), ***complete physical examination*** (Blood Pressure before and after HD, Heart rate, Mean ultra-filtration, Body mass index and Volume of 24 h Urine Output), ***laborator investigation*** (CBC, AST, ALT, serum albumin, serum creatinine, urea, before and after HD, Sodium, potassium, Calcium, Phosphorus and uric acid, Serum iron, ferritin and Transferrin saturation, Intact PTH, Serum CRP) and ***Calculation of residual renal function.***

Statistical analysis data were collected, tabulated, statistically analyzed using an IBM personal computer with Statistical Package of Social Science (SPSS) version 20 and Epi Info 2000 programs, where the following statistics were applied.

Descriptive statistics: in which quantitative data were presented in the form of mean (□**),** standard deviation **(SD)**, range, and qualitative data were presented in the form numbers and percentages **(%)**.

Analytical statistics:

- **Chi- squared test (χ^2)** was used to study association between two qualitative variables,
- **Student's t- test** is a **test** used for comparison between two groups having quantitative parametric variables.
- **Mann-Whitney test** is a test of significance used for comparison between two groups not normally distributed having quantitative variables.
- **Fisher's exact test** for 2 x 2 tables when expected cell count of more than 25% of cases was less than 5.
- For comparing the same group on different times **Paired T test** was used for parameter quantitative variables and **Wilcoxon** test was used for non parametric data. The level of significance of our data were 95%, so, P-value of (>0.05) was considered not statistically significant, P-value of (≤0.05) was considered statistically significant; P-value of (≤0.001) was considered statistically highly significant.

3. Results

During this study 73patients on chronic haemodialysis divided into two groups and comparison in between groups according demographic data (age, sex) shows no significant difference and revealed that mean age of HD patients Group 1 is,(45.6 ± 18.2) (54.2%) of them are males and mean age of HD patients Group 2 is (47.5±14.69) (59.2%) of them are males.

This study revealed that the commonest cause of ESRD is hypertension (45.8%) in Group 1(65.3%) in Group 2. (Figure1)

Mean heart rate of Group 1 is (77.4) and its (77.4) for Group 2 Mean systolic BP for Group 1 before the session is (137.9) and after the session is (120.8). In Group 2 before the session is (136.9) and after the session is (127.9) which show no statistically significance between both groups.

Mean diastolic BP for Group 1 before the session is (81.3) and after the session is (72.5). In Group 2, it's (82.4) before the session and (78.6) after the session with no statistically significance between both groups.(Figure2)

Also the study shows the Mean ultrafiltration rate by liters in Group 1 of residual renal function is (1.92L) and in Group 2 of non residual renal function is (2.95L).(table1)

Regarding to kidney function test (creatinine &urea) shows that:

- Creatinine before the session is (8.3) in Group 1and (11.2) in Group 2. Creatinine after the session is (3.5) in Group 1 and (4.6) in Group 2 that shows statistically significance between both groups.
- Blood urea after &before the session shows no statistically significance between both groups. (figure 3)

Table 1: comparison between both groups regarding mean ultrafiltration in patients (no=73).

Items	Patients with residual urine (NO=24)	Patients without residual urine (NO=49)	Test of sig. p-value
Mean ultrafiltration			
- Mean ±SD - Range	1.92±0.79 0-3	2.95±1.2 0-5	**Mann Whitney=3.7 p=0.00**(<0.001)**

Regarding to serum albumin no any significant difference between groups regarding serum albumin. The mean serum albumin is (3.9) in Group 1 and (4.2) in Group 2. (Table 2)

There is increase in sensitivity of CRP protein in both groups. It is 33.3% positivity in Group1and 61.2% positivity in group 2. (Table 5)

Results regarding to hemoglobin, Serum iron and TSAT show statistically significant difference between

groups. No statistically significant difference between groups regarding to ferritin. (table 4)

It also shows statistically significant difference between both groups regarding serum calcium (8.2) in Group 1 and (9.2) in Group 2. (Anuric patients are less hypocalcemic). Serum phosphors is (5.2) in Group 1 and (5) in Group 2. Regarding intact para thyroid hormone, it shows statistically significance difference between both groups. It is (400.9) in Group 1 and (719.2) in Group 2. (Table 3)

Table 2: comparison between both groups regarding albumin level in patients (no=73)

Items	Patients with residual urine (NO=24)	Patients without residual urine (NO=49)	Test of sig. p-value
Albumin			
- Mean ±SD - Range	3.9±0.63 3-5.2	4.2±0.46 2.8-5	**t=1.7** **p=0.14(>0.05)**

Table 3: comparison between both groups regarding calcium & & phosphorus & intact PTH in patients (no=73)

Items	Patients with residual urine (NO=24)	Patients without residual urine (NO=49)	Test of sig. p-value
Calcium			
- Mean ±SD - Range	8.2±0.96 5.9-11	9.2±1.1 7.3-13	**t=3.9** **p=0.00**(<0.001)**
Phosphorus			
- Mean ±SD - Range	5.2±0.95 3.5-6.7	5.0±1.2 2.5-8.5	**t=0.88** **p=0.38(>0.05)**
Intact PTH			
- Mean ±SD - Range	400.9±134.5 132-670	719.2±370.1 74-1560	**Mann Whiney=3.8** **p=0.00**(<0.001)**

Table 4: comparison between both groups regarding iron profile patients (no=73)

Items	Patients with residual urine (NO=24)	Patients without residual urine (NO=49)	Test of sig. p-value
Hemoglobin			
- Mean ±SD - Range	10.9±0.36 10.5-11.5	9.8±2.2 9.8-12.9	**t=3.7** **p=0.001*(< 0.05)**
Serum iron			
- Mean ±SD - Range	85.4±28.2 42-130	61.6±41.9 30-235	**Mann Whiney=2.8** **p=0.004*(<0.05)**
Serum ferritin			
- Mean ±SD - Range	259.7 ±187.6 115-672	317.6±264.6 10-1000	**Mann Whiney=0.45** **p=0.66(>0.05)**
TSAT			
- Mean ±SD - Range	44.1±10.2 26-65	34.6±17.4 13.5-100	**Mann Whiney =2.59** **p=0.011*(<0.05)**

Table 5: comparison between both groups regarding C reactive protein in patients (no=73)

Items	Patients with residual urine (NO=24)		Patients without residual urine (NO=49)		Test of sig. p-value
CRP					
- Positive - Negative	8 16	33.3 66.7	30 19	61.2 38.8	**X^2= 3.9** **P=0.046*(<0.05)**

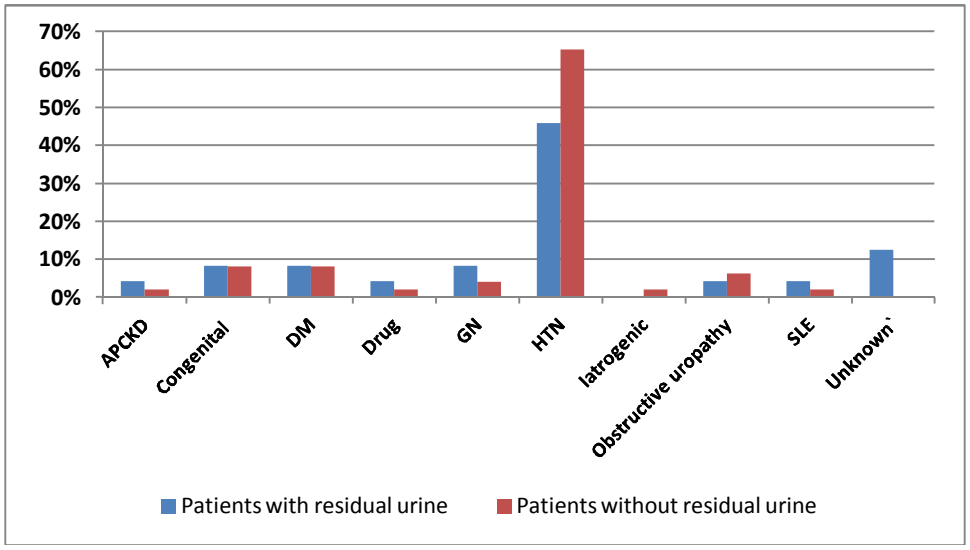

Figure (1) shows the distribution of the studied groups as regard cause of ESRD. The most common cause is hypertension in both group.

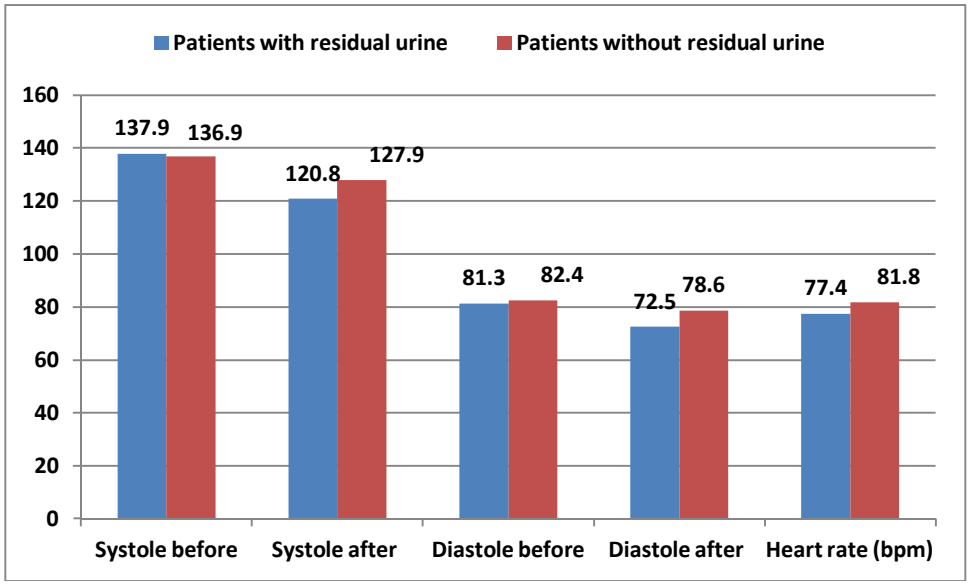

Figure (2) compares both group in blood pressure (systole & diastole) before and after the session and heart rate.

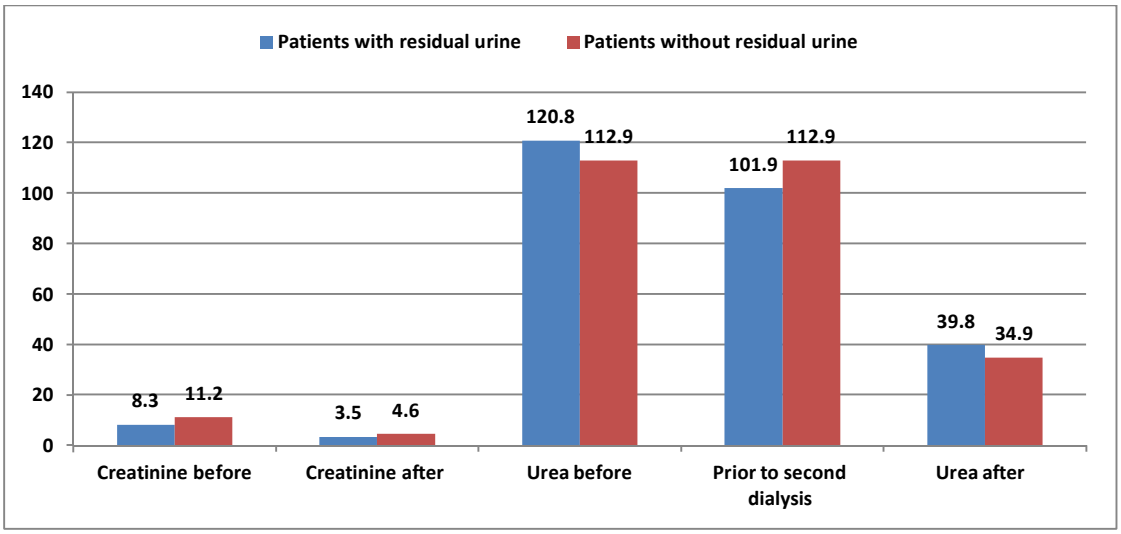

Figure (3) Compare between both groups according to serum creatinine (after & before the session) serum urea (after & before the session and prior to the next session)

4. Discussion

Regarding to blood pressure our result in agreement with Sikorska ***et al.*** **[6]** (a study of 44 patients placed into three, subgroups depending on volume of residual diuresis (group A ≤ 500; group B 600–1900; and group C ≥ 2000 mL/day) comparable arterial systolic blood pressure values (group A 137.1 ± 23.2 mmHg, group B 134.3 ± 13.9 mmHg, and group C 138.6 ± 18.1 mmHg) and diastolic blood pressure values (group A 85.2 ± 13.8 mmHg, group B 80.9 ± 11.2 mmHg, and group C 79.6 ± 11.1 mmHg) were observed in each group. No statistically significant differences between groups and no significant difference in the amount of antihypertensive medicines received. this study confirm our results regarding ultrafiltration rate and kidney function test that show according to ultrafiltration rate that Group A (diuresis ≤500 m L/week demonstrated the highest daily ultrafiltrationin comparison with group C (C ≥ 2000 mL/day) (1592 ± 636 ml vs. 967 ± 551 ml in group C; $p = 0.011$) and regarding serum creatinine show The group with the largest diuresis (group C) was characterized by the highest total weekly creatinine clearance (115.4 ± 35.2 L/week) in comparison with the remaining two groups (82.4 ± 17.7 L/week in group B and 52.2 ± 14.4 L/week in group A; $p = 0.006$ and $p = 0.001$, respectively). **[6]**

Regarding serum albumin our results handby with ***Borges et al.***[7] which found that serum albumin concentrations were not different between groups in a study enrolled 80 patients with CKD undergoing haemodialysis Also, this study in harmmony with ***Gama-Axelsson et al[8]*** albumin levels among patients with normal nutritional status did not differ between both groups of patients.

Regarding CRP this finding is were agreed with ***Borges et al (2016) and Kumar & Shobharani (2015)*** which found that *There was a significant relationship between reduced GFR and Hs CRP levels which suggests that there is inflammatory activity in the CKD patients* This results also were consistant with **(Pecoits. et al., 2003)** study in pre-dialysis chronic kidney disease patients has reported a similar inverse relationship between renal function and pro-inflammatory mediators. this could be due to immune dysregulation and inflammatory activation in CKD as Uremic milieu produces oxidative stress[9] and carbonyl stress[10] that are highly pro-inflammatory. Decreased renal clearance clearly accounts for higher levels of circulating cytokines, although increased production has also been described.[11] Decreased antioxidants because of the oral intake or the level of some antioxidants is lower than normal in both CRF and ESRD patients.

Regarding anemia and iron profile This results are in agree with Sikorska et al. **[6]**another observation also present in this study, anemia connected with lower erythropoietin production,**[12]** can be an additional factor placing strain on the circulatory system in patients with minimal residual renal function.

A relation between RRF and erythropoiesis-stimulating agent (ESA) requirements that were lower in HD patients with RRF in a single-center retrospective study, possibly because of decreased ESA resistance, but these observations were not adjusted for potential confounders.**[13]** In a recent study, erythropoietin dose requirements were significantly lower in patients with urinary output 1

year after initiation of HD as compared with those without.**[14]**

As regard iron profile, our results in agree with ***Alves et al***, **[15]** another cause of anemia and erythropiotine resistance in dialysis patient is due to iron deficiency and explain this as the deficiency or reduction of total iron stores can occur due to an increase in demand of this nutrient during the production of red blood cells in the bone marrow. This absolute iron deficiency may also be related to the dialysis procedure, which promotes premature destruction of red blood cells (hemolysis), but also due to gastrointestinal bleeding, or frequent laboratory blood tests and surgeries, which patients can be submitted to.**[16]** Furthermore, transferrin saturation and serum ferritin levels may help to distinguish between conditions associated with deficiency or impairment of availability of iron.[17]

Results disagree with results of **[18]** study of 57.1% (*N*=44) of the patients were anuric Regarding Rhee et al the biochemical CKD-MBD factors, serum phosphate, Ca/P product, were significantly lower and $1,25(OH)_2D_3$ levels were significantly higher in the nonanuric patients, although the frequency of prescribed medications for phosphate control was not significantly different between groups. However, serum iPTH and 25(OH)D levels were not different, according to the RRF status.

The significance of RRF in CKD-MBD in HD patients was first described by ***Viaene et al***.[19] In their study, RRF was found to be an important determinant of FGF-23 and phosphate control in HD patients. Furthermore, ***Penne et al*** **[20]** reported in their study that GFR was negatively correlated with the phosphate binder dose in HD patients, and a GFR of >4.13 mL/minute/1.73 m^2 was an important predictor of adequate phosphate control.

5. Conclusion

RRF is important to both hemodialysis (HD) and PD patients preservation of RRF confers a survival advantage for dialysis patients. It is time to realize that residual renal function is a very valuable asset to patients on dialysis and that the important goal to preserve residual renal function should continue even after patients are started on dialysis**.**

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