# Impact of Residual Kidney Function on Mineral Bone Disorders in Hemodialysis Patients

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**Abstract: Background:** Previous studies have demonstrated that mineral bone disorders are major complications of end stage renal disease patients on regular hemodialysis. Residual kidney function could affect severity of complications of hemodialysis and bone biomarkers. We hypothesized that preservation of residual kidney function may have impact on bone mineral disorders in chronic hemodialysis patients. **Methods**: The study was done on 100 patients on regular hemodialysis, three sessions per week, in dialysis unit of Shebin ElKom Teaching Hospital. Patients were divided into three groups according to urine output (UOP) in 24 hours, **group 1** (UOP > 50 ml \ 24h), **group 2** (0 < UOP < 50 ml\ 24h), **group 3** (no UOP) and we measured corrected calcium, phosphorus, iPTH, hemoglobin level and calculated KT\V per session then compared these parameters with residual kidney function (RKF) which was calculated by Daugirdas method. Residual kidney function ($K_{ru}$)=(UUN÷SUN)×urine flow rate (ml\min) (Handbook of Dialysis, 5th edition, 2015). **Results**: All three groups were compared regarding corrected Ca, phosphorus, iPTH, hemoglobin level, Kt\v and residual kidney function. There was a significant difference between three groups regarding hemoglobin level, kt\v, corrected Ca, iPTH and residual kidney function with P value (0.006), (0.001), (0.001), (0.032) and (0.001) respectively, on the other hand, there was no significant difference between three groups regarding phosphorus with P value (0.838). **Conclusion:** Residual kidney function is an important tool to assess remaining of kidney function and may improve bone mineral disorders if it is preserved, but still the phosphorus out of its control and may be affected by other factors need to be more studied.
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## 1. Introduction:

Residual kidney function (RKF) may confer a variety of benefits to patients on maintenance dialysis. RKF provides continuous clearance of middle molecules and protein-bound solutes. Whereas the definition of RKF varies across studies, interdialytic urine volume may emerge as more appropriate calculations. **(Mathew AT, Fishbane S, Obi Y, 2016).**

Observational studies have shown that preservation of residual renal function (RRF) in dialysis patients is an independent prognostic factor in patient survival and quality of life **(Plantinga LC et al, 2010).** There is an increased focus on preserving RRF in hemodialysis patients **(Perl J, Bargman JM, 2009).**

Whereas the role of residual renal function for survival is well recognized in the peritoneal dialysis population, it has not received much attention in the hemodialysis population. Another study showed that residual renal function contributes significantly to improved outcomes in hemodialysis patients and that efforts to preserve it are warranted **(Vilar et al 2009),**.

The benefits of RKF are hypothesized to be mediated by improved control of volume, minerals, and electrolytes; less inflammation; and greater clearance of protein-bound solutes and middle molecules. HD is used only intermittently whereas native kidney function is continuous. For this reason, even a small amount of residual function reduces plasma levels of solutes cleared poorly by HD, such as low molecular weight proteins like B2-microglobulin and protein-bound solutes. In HD patients, RKF allows for lower ultrafiltration volumes during each dialysis session, resulting in less intradialytic hypotension and myocardial stunning.

Mineral and bone disorder (MBD) affects the majority of patients with chronic kidney disease and is characterized by imbalances in serum levels of parathyroid hormone (PTH), calcium (Ca), and phosphorus (PO). **(Mark D, Vasily Belozeroff, Karen Smirnakis, 2008).**

Preserving residual kidney function in hemodialysis patients may contributes to more control of MBD and good outcomes of hyperphosphatemia hence, reducing calcification and mortality among hemodialysis patients. **(John T. Daugirdas, Glenn M. Chertow, Brett Larive,et al 2012).**

RKF contributes to overall clearance in both PD and HD patients, with related better patient survival

and quality of life. Clinical management and research efforts should consider a focus on strategies to preserve RKF. Based on a critical literature review, suggestion of the following considerations for the preservation of RKF in all patients newly started on HD as avoiding nephrotoxic drugs, control blood pressure, avoid intradialytic hypotension and adjustment of hemodialysis prescription**, (Mathew AT, Fishbane S, Obi Y, 2016 ).**

## 2. Materials and Methods:

### Study Design

This is a cross sectional study. Study populations was selected from patients on regular hemodialysis sessions in dialysis unit of Shebin ElKom teachning hospital. The was conducted on 100 regular hemodialysis patients to evaluate the impact on residual kidney function on bone mineral disorders regarding corrected Ca, phosphorus and iPTH.

Patients were divided according to urine output ( UOP ) in 24 hours into three groups, **group 1** ( UOP > 50 ml \ 24h), **group 2** ( 0 < UOP < 50 ml\ 24h), **group 3** ( no UOP ).

### Study Population

All patients >18 years of age, clinically stable ESRD patients on regular hemodialysis for at least 3 months before study, on treatment of phosphate binders,vitamin D or calcimimetics ( if indicated ). We excluded patients on ACEIs or ARBs and those who had a recent history of hospitalization or unstable hemodynamic status.

All patients were subjected to informed consent, either thorough or full history taking and clinical examination including information on age, sex, duration on hemodialysis and medication history (e.g.ACEIs, ARBs, phosphate binders, vitamin D or calcimimetics). They were also subjected to routine laboratory analysis with special concern to hemoglobin level, corrected calcium, serum phosphorus, iPTH and calculation of Kt\v per session by Daugirdas method. We measured residual kidney function (Kru) in patients with UOP by following equation:

Residual kidney function ($K_{ru}$) = ( UUN ÷ SUN ) × urine flow rate (ml\min) ( Handbook of Dialysis, 5th edition,2015 )

Where UUN was urine urea nitrogen concentration in all urine collected during 24-hours period of interdialytic interval, SUN was estimated by mean serum urea nitrogen during the 24-hours collection period and calculated by: 90 % of Pre-dialysis Serum Urea Nitrogen concentration prior to a first of week session and Urine flow rate was amount of all urine (ml) which was collected during day \ 24 hours ( 1440 minutes ).

### Statistical Analysis

Statistical analyses were performed using the SPSS software version 22.0 (SPSS Inc, Illinois). Patient demographic characteristics were presented as mean and standard deviation for continuous variables with normal distribution, median and interquartile range for continuous variables with non-normal distributions and as proportions (percentages) for categorical variables. For continuous variables comparison between the three population subgroups was done by One-way ANOVA test, followed by Post Hoc (Tukey) test whenever significant difference is found. Simple two- or three-group comparisons were performed using $\chi^2$ (Chi-square) test for categorical variables. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So a P value lower than 0.05 was considered significant.

## 3. Results

The study population consisted of 100 consecutive patients on regular hemodialysis sessions, three times per week divided into three groups according to urine output (UOP) in 24 hours, **group 1** ( UOP > 50 ml \ 24h) n=36, **group 2** ( 0 < UOP < 50 ml\ 24h) n=10, **group 3** ( no UOP ) n=54. Table 1 shows that there was no statistically significant difference between the three studied groups as regard to age and sex ($p > 0.05$).

Table 2 shows comparison between the three studied groups regarding hemoglobin level, kt\v, corrected Calcium, phosphorus, iPTH and residual kidney function.

There was statistically significant difference between the three studied groups regarding hemoglobin level with mean of (9.4), (10.4) and (8.89) respectively with P value (0.006). Post Hoc analysis revealed statically significant difference as regard to hemoglobin level between groups 2 & 3 ($p < 0.006$). While there was no significant difference between group 1 and any of either Group 2 or 3.

While as regard Kt\v, revealed significant difference between three groups with mean of (1.6), (1.4) and (1.08) respectively with P value (0.001). post Hoc analysis revealed highly statistically significant between group 3 and group 1 & 2 of patients ($p < 0.001$). While there was no significant difference between group 1 and group 2.

There was statistically significant difference between the three studied groups regarding corrected calcium with mean of (10.3), (10.5) and ( 9.7) respectively with P value (0.001) which on Post Hoc analysis revealed statically significant difference between groups 3 and 1 & 2 ($p < 0.001$). While there was no significant difference between group 1 and group 2.

There was no statistically significant difference between the three studied groups regarding serum phosphorus with p value (0.838).

There was statistically significant difference between the three studied groups regarding iPTH with mean of (230.3), (1000) and ( 619.6) respectively with P value (0.032). Post Hoc analysis revealed statically significant difference between group 1 and group 2 & 3, while there was no significant difference between group 3 and group 2. There was a significant difference between group 1 and group 2 regarding residual kidney function with mean of (1.3) and (0.076) respectively with P value (0.001).

**Table (1):** Comparison between different study groups as regards age & sex

| Socio-demographic data | The studied groups | | | | |
|---|---|---|---|---|---|
| | Group 1 (N=36) | Group 2 (N=10) | Group 3 (N=54) | K | P value |
| **Age (years)** | 51.9±10.8 | 49.45±13.27 | 48.45±13.27 | 0.625 | 0.536 |
| **Sex** | No % | No % | No % | 1.5* | 0.46 |
| | 20 55.6 | 6 60.0 | 24 44.4 | | |
| | 16 44.4 | 4 40.0 | 30 55.6 | | |

CHI SQUARE test. K ( kruskal wallis test ), P > 0.05 (Insignificant ), P ≤0.05 (Significant), P < 0.001 (Highly Significant )

**Table (2):** Comparison between the different groups as regards Hb level, Kt\V, Corrected Calcium, Phosphorus and Residual kidney function

| LAB | The studied groups | | | | | |
|---|---|---|---|---|---|---|
| | Group 1 (N=36) | Group 2 (N=10) | Group 3 (N=54) | K | P value | POST HOC |
| **Hb (mg/dl)** | **9.4±1.6** | **10.4±0.85** | **8.89±1.6** | **10.2** | **0.006** | **P1=0.085 P2=0.108 P3= 0.006** |
| **Kt/V** | **1.6±0.34** | **1.4 ±0.34** | **1.08 ±0.33** | **45.8** | **0.001** | **P1=0.183 P2=0.001 P3=0.001** |
| **Corrected Calcium** | **10.3 ±0.73** | **10.5 ±1. 05** | **9.7±0.78** | **14.5** | **0.001** | **P1=0.503 P2=0.001 P3=0.004** |
| **Phosphorus** | **5.1±1.3** | **5.2±1.4** | **5.3±1.5** | **0.35** | **0.838** | |
| **iPTH** | **230.3±146.6** | **1000±1364.8** | **619.6±742.0** | **6.9** | **0.032** | **P1=0.002 P2=0.011 P3=0.114** |
| **Residual kidney function** | **1.3±1.2** | **0.076±0.044** | **----------** | **4.7** | **0.001** | |

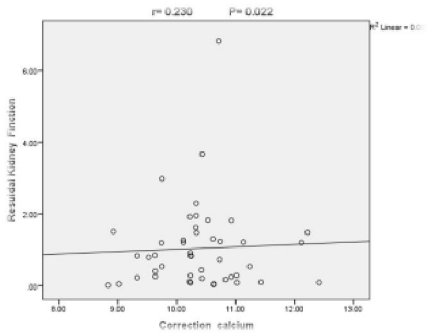


**Figure (1):** Correlation between residual kidney function and corrected Ca.

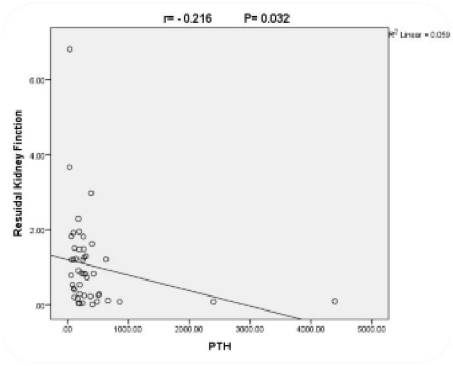


**Figure (2):** Correlation between residual kidney function and iPTH

## 4. Discussion

Mineral and bone disorders, characterized by abnormal serum concentrations of calcium, phosphorus, intact parathyroid hormone, and alkaline phosphatase, are common complications in patients with CKD, especially in those with ESRD **[ (KDIGO. 2009)].** However, those abnormalities may be attenuated in patients on hemodialysis with substantial residual kidney function who maintain greater solute clearance **(Mathew AT, et al. 2016).**

Hence, we hypothesized that maintenance of RKF in patients on regular hemodialysis will help in sustaining a favorable biochemical profile of MBD. The aim of this work was to evaluate the impact of residual kidney function on markers of mineral bone disorders (Ca, PO4 and iPTH ) in chronic hemodialysis patients.

In our study we found that the mean serum iPTH level of the patients was 230.3 ± 146.6 pg/mL in group 1, 1000 ± 1364.8 pg/mL in group 2, and 619.6 ± 742.0 pg/mL in group 3. The comparative study between the three groups shows a statistically significant difference (p value of 0.032) with a significant weak correlation between RKF and serum iPTH level and this was in agreement of Nii-KoNo et al study who demonstrated that is partly due to the diminished PTH receptor expression of osteoblast in the uremic milieu **(Nii-Kono T, et al. 2007).** However, these abnormalities in the uremic milieu are likely to be less severe among patients with substantial RKF compared with those with little or no RKF **(Mathew AT, et al. 2016).**

In our study we found that the mean Hb level of the patients was 9.4 ± 1.6 gm/dL in group 1, 10.4 ± 0.85 gm/dL in group 2, and 8.89 ± 1.6 gm/dL in group 3. The comparative study between the three groups shows a high statistically significant difference (p value of 0.006) and this was in agreement of what was previously noted by Wang AY and Lai KN in there study as they noted a relation between decline of RRF and more severe anemia and increased ESA resistance in HD patients **(Wang AY and Lai KN. 2006)**.

In our study we found that the mean Kt/V level of the patients was 1.6 ± 0.34 in group 1, 1.4 ± 0.34 in group 2, and 1.08 ± 0.33 in group 3. The comparative study between the three groups shows a high statistically significant difference (p value of 0.001).This result was in agreement of 2006 updates on the KDOQI clinical practice guidelines which underscored that the cutoff value of 1.2 for minimum Kt/V can be applied to patients with little or no RKF since it was derived from studies excluding patients with RKF or those assuming no RKF among participants **(Hemodialysis Adequacy Work Group. 2006).**

In our study we found that the mean corrected serum calcium level of the patients was 10.3 ± 0.73 mg/dL in group 1, 10.5 ± 1.05 mg/dL in group 2, and 9.7 ± 0.78 mg/dL in group 3. The comparative study between the three groups shows a high statistically significant difference (p value of 0.001) with a significant weak correlation between RKF and corrected serum calcium level, while Previous studies have shown the fact that calcium is less likely to be affected by RKF than phosphorus. Recent calcium balance studies have consistently shown that calcium loads resulted in little or no increase in urinary calcium excretion, even in patients with CKD stages 3 and 4. Calcium may be excreted into the urine at even lower levels in patients with ESRD and low RKF **(Hill KM, et al. 2013).**

On the other hand, in our study we found that the mean serum phosphate level of the patients was 5.1 ± 1.3 mg/dL in group 1, 5.2 ± 1.4 mg/dL in group 2, and 5.3 ± 1.5 mg/dL in group 3. The comparative study between the three groups shows a statistically insignificant difference (p value of 0.838) with an insignificant correlation between RKF and serum phosphate level. This was against of what was described by Viaene et al who proved significance of RKF in CKD-MBD in HD patients **(Viaene L, et al. 2012).** In their study, RRF was found to be an important determinant of phosphate control in HD patients. Furthermore, Penne et al reported in their study that GFR was negatively correlated with the phosphate binder dose in HD patients, and a GFR of 44.13 mL/minute/1.73m2 was an important predictor of adequate phosphate control **(Penne EL, et al. 2011).** This difference between our study and other studies contributed to many factors as number of patients with urine output > 250ml\24h were lower than other studies.

**Study Limitations**

Although the number of patients enrolled in our study is relatively small, the results are quite comparable to larger studies. Duration of hemodialysis may have an important impact on residual kidney function but was not addressed in current study. A longer duration of follow up of residual kidney function with corrected calcium, phosphorus and iPTH may be better than a spot sample in only one month. Additionally, measurement of serum phosphorus may affected by diet of patients which was differed from one to another and affected also by efficacy and patency of vascular access of patient which in turn affects adequacy of hemodialysis, that may be differ regarding the type of access (hemodialysis catheter or AVF ) and the age of it. Finally, this study was observational and single-institutional in nature, which possibly restricted us from identifying and analyzing all potential confounding factors.

**Conclusion**

Based on the results of the current study, it can be concluded that residual kidney function has an impact on mineral bone disorder regarding corrected calcium and Ipth as if it maintained it may improve corrected calcium and Ipth, but this was not noticed regarding phosphorus. Although phosphorus is an important factor in pathogenesis of mineral bone disorder, maintaining residual kidney function failed to decrease its level in blood. limitations mentioned above and other prospective studies may have an answer to cause of this failure.

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