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Correlation Between Urea and Phosphate Reduction Ratios During Hemodialysis

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ABSTRACT

Objective: To compare the efficacy of serum phosphate and urea removal during hemodialysis.

Study Design: Correlational Cross-sectional study.

Place and Duration of Study: Combined Military Hospital, Peshawar, Pakistan from Jul to Dec 2020.

Methodology: Adult patients on maintenance hemodialysis for three months or more were selected by non- probability convenience sampling. Exclusion criteria included hemodialysis for acute kidney injury, the initial three sessions of maintenance hemodialysis in patients with end-stage renal disease and patients unwilling for inclusion in the study. All patients had blood samples collected for serum urea and phosphate before and immediately after completion of hemodialysis session using standard technique. Urea and phosphate reduction ratios were calculated and compared by linear regression.

Results: Hemodialysis sessions were monitored in 76 patients, including 54(71.05%) males and 22 (28.95%) females having mean age of 53.38±13.82 years. During the three-and-a-half-hour-long sessions, urea reduction ratio was greater than phosphate reduction ratio (70.14±11.60% vs 53.19±13.17% respectively). There was a moderate statistically significant correlation between the two (r=0.23; *p*=0.009). The urea reduction ratio was dependent on gender but not on type of vascular access. Phosphate reduction ratio was not dependent on gender or vascular access.

Conclusion: Phosphate reduction is not as effective as urea reduction during hemodialysis. Thus, other modalities are required for better control of serum phosphate levels amongst patients undergoing hemodialysis.

Keywords: end stage renal disease, hyperphosphatemia, renal dialysis, renal replacement therapy.

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INTRODUCTION

Management of chronic kidney disease and its related complications is one of the most challenging health problems worldwide. The disease prevalence in Pakistan is 16.6%–25%.[1] Estimated glomerular function rate (eGFR) below 60 ml/min/ 1.73m² requires steps to slow down disease progression, whereas eGFR below 15ml/min/ 1.73m² requires more aggressive management, including pre-emptive renal transplant or initiation of maintenance hemodialysis as suggested by clinical status of the patients. End-stage renal disease (ESRD) frequently compromises the quality of life and makes patients vulnerable to dependency on caregivers.[2] Hemodialysis is a costly treatment that drains resources and health care budget.[3] In resource-poor countries like Pakistan, we face the obstacle of overcoming the inevitable complications associated with maintenance hemodialysis.

The deterioration in renal function leads to accumulation of uremic toxins, categorized into three subtypes: small water-soluble, small lipid-soluble and middle molecules. A high unbalanced level of small molecules i.e., inorganic phosphorous is the major trigger for development of mineral bone disease, a menacing complication of end-stage renal disease. Sixty percent of dietary phosphate is absorbed through the gastrointestinal tract and of this 95% is eliminated through kidneys.[4] As kidneys fail to function, the long-term effect of hyperphosphatemia will lead to secondary hyperparathyroidism and vascular calcification.[5] There is evidence to suggest an 18% increased risk of all-cause mortality and 67% increase in cardiovascular disease with each 1 mg/dl rise in serum phosphate levels.[6]

There are three main modalities for controlling hyperphosphatemia in CKD: initially through phosphorus-restricted diet, augmented by oral phosphate binders in CKD 3- 5ND and additionally by maintenance hemodialysis in end-stage renal disease. Despite all this, many patients fail to achieve targets for serum phosphate levels. The prevalence of hyperphosphatemia is as high as 35-69% in maintenance hemodialysis regardless of the use of phosphate binders.[7]

One of the ways to measure hemodialysis adequacy is urea reduction ratio (URR). It is a known

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fact that there may be differences in intradialytic phosphate and urea removal kinetics.[8] This means that the reductions in these two might not correlate well with each other. Therefore, this study was designed to determine the relationship between urea and phosphate reduction ratios. The results of this study would be a helpful contribution to improved management of hyperphosphatemia in dialysis-dependent patients by focusing on better hemodialysis adequacy.

METHODOLOGY

The correlational cross-sectional study was conducted in Dialysis Unit, Combined Military Hospital Peshawar, Pakistan, from July to Dec 2020. Approval from Ethical Review Committee of Combined Military Hospital Peshawar was sought via letter reference No.[4] Study participants were selected using a non-probability convenience sampling technique. The sample size calculation was done using online calculator available on Statistics Kingdom website.[9] Keeping the power at 80%, significance levels at 0.05, and effect size 0.14 (small), a minimum sample of 51 patients was required for this study.

Inclusion Criteria: Both male and female patients, aged 18 years or more, on maintenance hemodialysis for ESRD, were selected as study participants.

Exclusion Criteria: Hemodialysis for acute kidney injury, the initial three sessions of maintenance hemodialysis in patients with ESRD, and patients unwilling to participate in this study were excluded.

A written informed consent was taken from all the patients before data collection. Demographic details, type of vascular access (tunneled cuffed catheter or arterio-venous fistula), duration of hemodialysis, and cause of ESRD were recorded. Blood samples for serum urea and phosphate levels were collected from the arterial port immediately before and after mid-week hemodialysis sessions and analyzed using a COBAS C 501 fifth-generation chemistry analyzer. Hemodialysis was conducted on Fresenius S4008 machine for 3.5 hours on all patients, with blood pump speed of 300 ml/minute, a dialysate flow rate of 500 ml/ minute, and ultrafiltration volumes to achieve dry weight. Fresenius F8 HPS dialyzers (polysulfone membrane with an effective surface area of 1.8m^2) were used for this study.

Data was analyzed using Social Package for Statistical Sciences (SPSS) version 23. Quantitative variables were described as mean and standard deviation, and qualitative variables were described as frequencies (and percentages). Correlation between urea reduction ratio (URR) and phosphate reduction ratio (PRR) was conducted. The effect of gender and type of vascular access on URR and PRR was determined through an independent samples t-test. $p<0.05$ was considered significant.

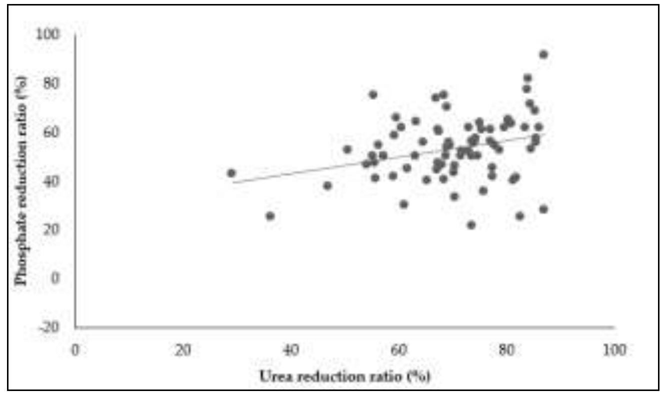

Figure-1: Correlation Between Urea and Phosphate Reduction Ratios

RESULTS

A total of 76 patients participated in the study. These included 54(71.05%) males and 22(28.95%) females with a mean age of 53.38±13.82 years. Baseline characteristics are shown in Table-I.

Table-I: Baseline Characteristics (n=76)

Variable		Value
Age (years)		53.38±13.82
Hemodialysis vintage (months)		19.50 (12.00-36.00)
Gender	Male	54(79.1%)
	Female	22(28.9%)
Vascular access	Arteriovenous fistula	62(81.6%)
	Tunneled cuffed catheter	14(18.4%)
Cause of ESRD*	Diabetes mellitus	34(44.7%)
	Hypertension	15(19.7%)
	Ischemic heart disease	12(15.8%)
	Glomerulonephritis	07(9.2%)
	NSAIDs induced nephropathy	04(5.3%)
	Nephrolithiasis	02(2.6%)
	Eclampsia	01(1.3%)
	CA prostate	01(1.3%)

**End Stage Renal Disease (ESRD)*

Mean serum urea levels were 23.29±7.13mmol/l and 6.84±3.35mmol/l before and after hemodialysis, respectively. Mean serum phosphate levels were 1.93±0.60 mmol/l and 0.89±0.36 mmol/l before and after hemodialysis. Mean URR was 70.14±11.60%, and PRR was 53.19±13.17%. The latter was underestimated by 24.17%. A statistically significant moderate correlation was observed between URR and PRR. (r=0.23; *p*=0.009) (Figure-1). URR was higher in females, but there was no significant difference in PRR amongst the two genders (Table-II). The type of vascular access did not affect either URR or PRR (Table-III).

Table-II: Effect of Gender on URR and PRR (n=76)

	Male	Female	*p*-value
URR* (%)	67.69±12.30	76.16±6.71	0.003
PRR* (%)	51.84±13.28	56.50±12.56	0.157

**Urea Reduction Ratio (URR)*
**Phosphate Reduction Ratio (PRR)*

Table-III: Effect of Vascular Access on URR and PRR (n=76)

	Arteriovenous Fistula	Tunneled Cuffed Catheter	*p*-value
URR* (%)	71.40 ± 11.12%	64.59 ± 12.44%	0.076
PRR* (%)	53.40 ± 13.56%	52.24 ± 11.69%	0.747

**Urea Reduction Ratio (URR)*
**Phosphate Reduction Ratio (PRR)*

DISCUSSION

The findings of the study show a significant correlation between URR and PRR. URR is influenced by gender of the patients but not by the type of vascular access. PRR remained unaffected both by gender and the type of vascular access.

Hemodialysis is the main treatment modality of renal replacement therapy in Pakistan, where renal transplant is expensive for underprivileged people. Additionally, renal transplant is complicated due to a lack of a cadaveric kidney transplant program, resulting in a shortage of donor kidneys. Despite that, only 40% of patients in Pakistan are fortunate enough to have access to dialysis centers.[10] Patients with ESRD require long-term hemodialysis to sustain life. Of them, majority are under dialyzed either due to missed hemodialysis sessions or intradialytic complications.[11] This has to be delivered in an adequate dose to be effective. One of the ways to measure adequacy of hemodialysis is the URR.

A study done by Abbas *et al.*, on 34 patients at Lahore,[12] showed that the phosphate removal was independent of URR or even Kt/V estimated by online clearance monitoring. These results were contrary to the findings of this study. URR was gender dependent in this study sample, as the female patients had higher values than males. A study done on 143 patients in Dar Es Salaam, Tanzania, showed results similar to this study.[13] Another similar study on 202 patients with ESRD in Iran also showed that females had a higher URR. However, half of the patients did not achieve the optimal goal of URR, i.e., 65% and above.[14]

Similarly, the effect of vascular access on URR was studied by Shahdadi *et al.*, on 133 patients from Iran.[15] Hemodialysis adequacy in this study was not dependent on the type of vascular access. These results were correspondent with those of this project. However, another study by Chand DH et al was done on 12,501 American patients showed higher URR amongst patients with arteriovenous fistulas as compared to those with central venous catheters.[16]

The effectiveness of phosphate removal in hemodialysis patients through different phosphate binders has been exclusively studied by Hannedouche T *et al.*, The study highlights that dietary phosphate restriction alone does not benefit patients. Phosphate-containing food is a vital source of dietary protein. Its lifelong restriction can lead to protein malnutrition. Meanwhile, phosphate used as an additive is 100% absorbed in the gastrointestinal tract.[17]

Phosphate removal is through a complex mechanism, being an inorganic solute present intracellularly. The theories regarding phosphate reduction being higher in the initial phase and remain constant or unchanged at the end of the hemodialysis session, contrary to urea reduction, which is removed throughout the session.[18] If the adequacy of hemodialysis is assessed by measuring URR alone, it is very much possible that adequate phosphate reduction might not take place, resulting in hyperphosphatemia. This study suggests that there is a statistically significant relationship between URR and PRR, which is coherent with the findings of the study conducted by Elias RM *et al.*, in Brazil on eight patients. The study showed that the URR is greater than PRR in conventional dialysis, and by increasing the duration of hemodialysis sessions, phosphate reduction can be achieved to the target goal.[19] The main reason for this phenomenon is the slow release of phosphate from the intracellular body stores during hemodialysis, so that it takes time for it to be removed through dialysis. A study done by Zupančič *et al.*, on another eight patients concluded that conventional hemodialysis is an ineffective way to deal with hyperphosphatemia and nocturnal hemodialysis is superior to conventional therapy.[20]

LIMITATIONS OF STUDY

A sample size, focusing on patients receiving free hemodialysis, has limited the generalizability of the results in other study settings. The confounding variables were not considered while studying the correlation between URR and PRR. Future research should focus on different study designs to assess the reduction ratios of urea and phosphate in controlling hyperphosphatemia in end-stage renal disease.

CONCLUSION

Intermittent hemodialysis is less effective in removing excess phosphate from the body, as compared to urea. This mandates the need for other strategies, such as oral phosphate binder and dietary restriction for the control of hyperphosphatemia in end-stage renal disease.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MB & ARA: Conception, study design, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

REFERENCES

1. Shafi ST, Saleem M, Anjum R, Abdullah W, Shafi T. Refusal of hemodialysis by hospitalized chronic kidney disease patients in Pakistan. Saudi J Kidney Dis Transpl 2018; 29(2): 401-408. https://doi.org/10.4103/1319-2442.229270
2. Arshad AR, Khan G, Amjad Z, Butt B, Islam F, Qayyum M, et al. Predicting quality of life in hemodialysis patients. Pak Armed Forces Med J 2019; 69(1): 175-181. https://www.pafmj.org/PAFMJ/article/view/2518
3. Mushi L, Marschall P, Fleßa S. The cost of dialysis in low and middle-income countries: a systematic review. BMC Health Serv Res 2015;15:506. https://doi.org/10.1186/s12913-015-1166-8
4. Elder GJ, Malik A, Lambert K. Role of dietary phosphate restriction in chronic kidney disease. Nephrology (Carlton) 2018; 23(12): 1107-1115. https://doi.org/10.1111/nep.13188
5. Kim JS, Hwang HS. Vascular Calcification in Chronic Kidney Disease: Distinct features of pathogenesis and clinical implication. Korean Circ J 2021; 51(12): 961-982. https://doi.org/10.4070/kcj.2021.0995
6. Zhang W, Du Q, Xiao J, Bi Z, Yu C, Ye Z et al. Modification and validation of the phosphate removal model: a multicenter study. Kidney Blood Press Res 2021; 46(1): 53-62. https://doi.org/10.1159/000511375
7. Wang M, Li H, Liao H, Yu Y, You L, Zhu J, et al. Phosphate removal model: an observational study of low-flux dialyzers in conventional hemodialysis therapy. Hemodial Int 2012; 16(3): 363-376. https://doi.org/10.1111/j.1542-4758.2012.00678.x
8. Debowska M, Wojcik-Zaluska A, Ksiazek A, Zaluska W, Waniewski J. Phosphate, urea and creatinine clearances: haemodialysis adequacy assessed by weekly monitoring. Nephrol Dial Transplant 2015; 30(1): 129-136. https://doi.org/10.1093/ndt/gfu266
9. Statisticss Kingdom. Regression and ANOVA - Sample Size Calculator. Melbourne: [Internet]. Available at: https://www.statskingdom.com/sample_size_regression.html
10. Anees M, Hameed F, Mumtaz A, Ibrahim M, Saeed Khan MN. Dialysis-related factors affecting quality of life in patients on hemodialysis. Iran J Kidney Dis 2011; 5(1): 9-14.
11. Arshad AR, Fahad M, Begum M, Ahmed T, Khan I. Is missing hemodialysis associated with short term morbidity and mortality in end stage renal disease? Ann King Edw Med Univ 2021; 27(4): 531-535. https://doi.org/10.21649/akemu.v27i4.4886
12. Abbas M, Saleem S, Rasool Z, Mahmood A, Mansur A. Phosphate clearance in End Stage Kidney Disease patients on Hemodialysis. J Pak Soc Intern Med 2024; 5(4): 729-734. https://doi.org/10.70302/jpsim.v5i4.2474
13. Somji SS, Ruggajo P, Moledina S. Adequacy of hemodialysis and its associated factors among patients undergoing chronic hemodialysis in Dar es Salaam, Tanzania. Int J Nephrol 2020; 2020: 9863065. https://doi.org/10.1155/2020/9863065
14. Rezaiee O, Shahgholian N, Shahidi S. Assessment of hemodialysis adequacy and its relationship with individual and personal factors. Iran J Nurs Midwifery Res 2016; 21(6): 577-582. https://doi.org/10.4103/1735-9066.197673
15. Shahdadi H, Balouchi A, Sepehri Z, Rafiemanesh H, Magbri A, Keikhaie F, et al. Factors affecting hemodialysis adequacy in a cohort of Iranian patients with end-stage renal disease. Glob J Health Sci 2016; 8(8): 50-56. https://doi.org/10.5539/gjhs.v8n8p50
16. Chand DH, Teo BW, Fatica RA, Brier M; Medical Review Board of The Renal Network, Inc. Influence of vascular access type on outcome measures in patients on maintenance hemodialysis. Nephron Clin Pract 2008; 108(2): c91-8. https://doi.org/10.1159/000113525
17. Hannedouche T, Fouque D, Joly D. Complications métaboliques en insuffisance rénale chronique : hyperphosphatémie, hyperkaliémie et anémie [Metabolic complications in chronic kidney disease: hyperphosphatemia, hyperkalemia and anemia]. Nephrol Ther 2018; 14(6S): 6S17-6S25. https://doi.org/10.1016/s1769-7255(18)30647-3
18. Elias RM, Alvares VRC, Moysés RMA. Phosphate removal during conventional hemodialysis: a decades-old misconception. Kidney Blood Press Res 2018; 43(1): 110-114. https://doi.org/10.1159/000487108
19. Sampaio MS, Ruzany F, Dorigo DM, Suassuna JH. Phosphate mass removal during hemodialysis: a comparison between eKT/V-matched conventional and extended dialysis. Am J Nephrol 2012; 36(2): 121-126. https://doi.org/10.1159/000338675
20. Zupančič T, Ponikvar R, Gubenšek J, Buturović-Ponikvar J. Phosphate removal during long nocturnal hemodialysis/hemodiafiltration: a study with total dialysate collection. Ther Apher Dial 2016; 20(3): 267-271. https://doi.org/10.1111/1744-9987.12435

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