ORIGINAL ARTICLE

Anemia and Mineral Bone Disorder in Patients with End Stage Renal Diseases on Maintenance Hemodialysis

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ABSTRACT

Background: Chronic kidney disease characterised by urinary disturbances or excretory kidney dysfunction, which is likely to result in functional nephron damage. Glomerulonephritis is an immune-mediated kidney inflammation that affects both the glomerulus and other parts of the kidney. The most common cause of end-stage renal disease is glomerulonephritis. The aim of this study to determine the anemia, mineral bone disorder and high low PTH level during hemodialysis.

Study Design: This was cross-sectional study and conducted in the Ali Fatima Hospital Lahore, for six months March 2022 to August 2022.

Materials and Methods: There were total 350 participants. The participants were selected by sampling technique were interviewed in the Khyber teaching hospital Peshawar. We analyzed dependent and independent variables. Data analysis statistically by SPSS 20 version.

Results: There were total 350 participants which include71.4% males and 29% females in this research. The majority of the participants were in the age group (40-60) years or (n=350) 87% in the hemodialysis. The majority participants were mean age 49.2 ± 0.59 years. The participants were 69% financially depend upon family dialysis. The dialysis frequency of patients about 76% thrice per week and 24.2% were on twice per week. The hemoglobin level was <11 g/dL or mean 12.19±2.65 g/dL which show significantly reduced Hb level. The mean value of serum calcium, sodium, phosphorous and parathyroid levels in bone diseases were 165.40±6.91, 6.675±0.79, 6.89±2.64, and 255.63±233.71, which significantly changed in hemodialysis patients. Anti HCV is 80% positive in hemodialysis patients as compared to general population.

Conclusion: The participants who suffered to maintained hemodialysis for > 3 months, majority have low level of Hb which cause anemia, low PTH which associate with the mineral bone diseases and also reduced serum Ca, P, k, Na and albumin level.

Keywords: End stage renal disorder (ESRD), chronic kidney disorder (CKD).

INTRODUCTION

Hemodialysis is a synthetic cleaner of blood that utilizes a semipermeable membrane to monitor and control the amounts of essential elements such as nutrients, minerals, calcium, potassium, sodium, and bicarbonate salts. Mineral deficiency occurs frequently in hemodialysis patients due to dietary restrictions and the withdrawal of essential minerals from the blood, because there is no regulatory oversight in mineral reabsorption. Hemodialysis is linked to a variety of kidney disorders, including chronic kidney disease, diabetes, glomerulonephritis, and renal failure, all of which can ultimately led to end-stage renal disease. Chronic kidney disease that is characterized by urinary disorders or injury to excretory kidney dysfunction, likely to result in functional nephron damage. Glomerulonephritis is a type of immune-mediated kidney inflammation that impacts the glomerulus as well as other parts of the renal. Glomerulonephritis is the major cause of end-stage renal disease[1]. It necessitates either an Estimated Glomerular Filtration Rate of < 60ml/min or kidney damage indicators such as albuminuria. With a prevalence of 11% to 13% and affecting more above 71 years old people then diabetic and CKD has been linked to a vitamin D deficiency that is more common in people who suffered from renal transplants. CKD patients have greater rates of mortality and morbidity caused by cardiovascular diseases than a corresponding general public. The patients with end-stage kidney disease (ESKD) have a higher incidence of vascular calcification due to various hazard factors that trigger the phenotypic transformation of vascular smooth muscle cells, results in tissue mineral deposits and its linked with cardiovascular risk factors, including age, hypertension, diabetes, hyperphosphatemia, hyperparathyroidism, and excessive calcium intake[2]. Dialysis improves certain metabolic derangements caused by kidney failure including uremia, metabolic acidosis, hyperkalemia and other components like anemia and mineral bone disease need additional

medical management in the form of iron replacement, erythropoietin administration, calcium supplements, phosphate binders and active form of vitamin D3. Anemia is mostly normochromic and normocytic, and is due to decrease in erythropoietin production, decrease erythrocyte survival, bone marrow inhibition by uremic toxins, and deficiency of folate, iron, and vitamin B12. Anemia and CKD- MBD are important predictor of morbidity and mortality[3].

Hemodialysis and renal transplantation therapies required for the treatment of End stage renal diseases. Although hemodialysis is not a cure, it still does help ease many serious and occasionally fatal adverse reactions of CKD. Hemodialysis patients experience a higher hospitalization rate than the general public, which finally led to a variety of other problems like CKD, mineral bone diseases, anemia,, hypertension and other complications such as thrombosis, infection, ischemic steal syndrome, hematomas, heart failure, and prolonged bleeding, all of which necessitate frequent interventions as well as increased morbidity and mortality[4]. The average prevalence of ESRD in Pakistan is 100 patients per million population. Because of the high cost of therapy, the huge majority of these clients either don't undergo care or drop within the first three months. Low-income countries are continuously attempting to address the disparately increasing problem of kidney failure. Filtration process reusability is a widespread procedure in low-income countries to keep dialysis more affordable, and it has been demonstrated in various studies to lower costs by 32 to 34.6% [5]. For several years, the practice of reusing dialyzers has been challenged. Its benefits, such as expenditure, reduced waste treatment of waste, lower incidence of first-use disorder, and enhanced bioactivity, such as the possibility of infections, biochemical and immunologic reactions, inappropriate sterilization, changed membrane permeability, and performance loss[6]. The aetiology of chronic renal disease, where any renal function loss, the reason of the original injury, results to

glomerular hyper filtration with an increased single-nephron glomerular filtration rate, likely to result in vasculotoxic and inflammatory reactions, which are then involved in gradual glomerular damage, inducing local fibrosis and inflammation. The following aspects are part of the management control guidance for CKD patients: going to treat and trying to prevent kidney dysfunction and complications of CKD such as high blood pressure with prescription medications, blood glucose control, anemia, mineral bone disorder, metabolic alkalosis, heart disease, fatty acid management, and dietary management[7]. The gradual downturn in glomerular filtration rate distorts a wide range of biological processes as CKD develops. Anemia is frequently triggered by changes in hematological parameters, particularly red blood cell (RBC) indices[8]. Some other common side effect of CKD is worsening in mineral homeostasis, which expresses as alteration in serum phosphate and calcium concentrations as well as alters in serum concentrations of parathyroid hormone (PTH), tends to result in mineral bone disorder. A few researchers have suggested a relationship between anemia and mineral metabolism[9, 10].

METHODOLOGY

The study was cross-sectional. This study was conducted in the the Ali Fatima Hospital Lahore, from March 2022 to August 2022. Patients were selected using non probability purposive sampling. The total sample population of 350 include both gender. According to inclusion criteria all participants in the age group of (20-61) years, regular hemodialysis for >3 months and conduct hemodialysis twice and thrice per week. The flow rate of the dialysate was 500 ml/h, and the blood flow was 250–300 ml/min. The exclusion criteria were included heart failure, pregnancy and tumor. All the data were analyzed using Statistical Package for Social Sciences (SPSS) version 20. The different sociodemographic variables and medication were explored using chi square tests and an independent t test. A p-value of < 0.05 was considered as statistically significant. Khyber teaching hospital Peshawar, provided an ethical clearance letter.

RESULTS

This study included 350 participants (29%) female and (71.4%) male who were suffering end renal stage disorder to maintain hemodialysis. The majority participants were in the age group (40-60) years while mean age 49.2 ± 0.59 years. The participants were 69% financially depend upon family dialysis due to unemployment as well as low income. The causes of end stage renal diseases about 71.4% of patients had CKD. To measure the mean of hemoglobin, serum electrolytes which include Ca, P, Na, K and PTH and most of the patients were anemic with hemoglobin level and serum level reduced. Also to investigate serology test which include HBsAg and HCV in regular hemodialysis participants.

Table 1: Demographic characteristics among Hemodialysis patients shown in Table 1.

Variables	Categories	Frequency (n=350)N%
Gender	M	250 (71.4%)
	F	100 (29%)
Age	20-39	25 (7.1%)
	40-60	305 (87%)
	>61	20 (6%)
Occupational status	Employed	110 (31.4%)
	Unemployed	240 (69%)
Dialysis weekly	Twice	85 (24.2%)
	Thrice	265(76%)
Mean age ± S.D		49.2 ± 0.59 years
Mean dry weight		53.39 ± 10.65 kg
Mean height		155.09 ± 8.57 cm
Mean Body mass Index		25.29 ± 5.89 kg/m2
Mean Dialysis duration		>3 months

350 participants were included in this study and most of the participants were in age-group of 40–60 years and the mean age was 49.2 years.The dialysis frequency of participants about 76% thrice per week and 24.2% were on twice per week. The 69% patients were financially depend upon family dialysis were shown in Table 1.

Table 2: Evaluate the causes of end stage renal diseases in the participant

Causes of ESRD	Frequency (n=350)N%
DKD	50 (14.2%)
CKD	250 (71.4%)
CGN	20 (6%)
CTID	20 (6%)
ADPKD	10 (3%)

About 71.4% of patients had CKD of unknown causes of diseases. Diabetic kidney disease accounted for 14.2% of the cases were shown in (Table 2).

Table 3: Hemoglobin levels in the participant

Hemoglobin g/dL	Mean±SD	Frequency (n=350)N%	p-value
>11	6.76±0.12 g/dL	51 (15%)	0.221
<11	12.19±2.65 g/dL	299 (85%)	0.001***

Mean±SEM: ANOVA SPSS 20 Test *p<0.0; **<0.01; ***p<0.001:

The hemoglobin level was <11 g/dL or 85% participants which show significantly reduced. The mean hemoglobin was 12.19±2.65 g/dL and were anemic with hemoglobin level less than 11gm/dl. Iron stores were adequate in 85% patients with transferin saturation more than 20%.

Table 4: Evaluate the lab parameters like

Biochemical test	Mean±SD	p-value
Mineral Bone Dieases		
Serum Na	165.40±6.91	0.034
Serum k	6.675±0.79	0.033
Serum p	6.89±2.64	0.234
Serum ca	9.17±2.87	0.01**
PTH (pg/mL)	255.63±233.71	0.001***
TSTAT%	31.47±11.10	
RFT		
Serum urea (mg/dl)	155±63.91	0.451
Serum Creatinine (mg/dl)	7.92±4.51	0.543
Sereology		
HBsAg		
Positive	50 (14.2%)	0.043
Negative	300(86%)	0.765
Anti HCV		
Positive	280(80%)	0.001***
Negative	70 (20%)	0.136
Other Serum Test		
Serum Iron	101.17±57.44	0.01**
Serum TIBC	354.75±299.74	0.321
Serum Ferritin	587.20±355.40	0.001***

Mean±SEM: ANOVA SPSS 20 Test *p<0.0; **<0.01; ***p<0.001:

The mean value of serum potassium, sodium, phosphorous in bone diseases of the study patients were non significantly changed 165.40±6.91, 6.675±0.79, 6.89±2.64, and 255.63±233.71, but serum PTH and calcium which significantly reduced in hemodialysis patients. The parameters of RFT were also measured serum urea and creatinine 155±63.91 and 7.92±4.51 change. In this study, there was a high prevalence of Hepatitis C in hemodialysis patients as compared to Hepatitis B surface antigen positive patients. Anti HCV is 80% positive and significantly change in hemodialysis patients as compared to general population. Increase the rate oh HCV during dialysis, which increases with the dialysis period to maintain the hemoglobin by blood transfer. The mean ferritin was 587.20±355.40 μg/dL significantly change were shown in Table 4.

DISCUSSION

In this study mean age of the dialysis patients was 49.2 ± 0.59 years or 87% and most of the participants were male 71.4% then female. The mostly participants were low income or unemployed about 69% who depend upon family income for hemodialysis.

Anemia is a frequent complicating factor in hemodialysis-dependent CKD patients, with more than 90% of patients receiving an erythropoiesis-stimulating agent in various countries (ESA). Hemodialysis causes continued blood loss and deficient intestinal iron uptake. Anemia is a prevalent complicating factor of CKD as a result of factors such as erythropoietin insufficiency and depleted iron accessibility. In our study, we found that approximately 71.4% of hemodialysis patients must have CKD, with hb concentration of <11 g/dL or 85% significantly lower. The mean haemoglobin level was 12.192.65 g/dL, and the majority of the participants (85%) were anaemic, with haemoglobin thresholds < 11gm/dl. In 85% of sick people with transferin saturation significantly larger than 20%, iron stores were sufficient[11, 12].

Hemodialysis alteration in fairly commonly evaluated electrolytes, examines the connection between dialysate medication and such changes, and evolves preliminary diagnostic models to predict the HD alteration in serum electrolytes[13]. In our study, we also found that serum phosphorus, sodium, and albumin levels drop significantly after hemodialysis. On the basis of Kidney Disease Improving Global Outcomes guidelines, there appears to be a rebound decrease in serum calcium and Phosphate levels during hemodialysis[14, 15].

A major complication experienced by hemodialysis patients is chronic kidney disease-mineral-bone disorder. One of its major characteristics is irregular parathyroid hormone (PTH) metabolism, which expect to be treated to have either reduced PTH thresholds, as observed in dialysis patients, or elevated PTH concentration[16]. As just a consequence, in the latest research, we compared the results of hemodialysis patients who had reduced PTH levels, low bone retention and forming, a lowering in circulating calcium and phosphorus buffering, and thus death rates[17,18].

In this study, hemodialysis patients had a greater incidence of Hepatitis C than Hepatitis B surface antigen positive patients. This high prevalence of Hepatitis C might be a perception of the general population's high incidence of Hepatitis C. A increased incidence of Hepatitis C exposure to the virus during dialysis therapy, which tends to h the period of hemodialysis and the amount of blood donations necessary to maintain erythrocytes[19,20].

CONCLUSION

The participants who suffered to maintained hemodialysis for > 3 months, majority have low level of Hb which cause anemia, low PTH which associate with the mineral bone diseases and also reduced serum Ca, P, k, Na and albumin level. Therefore, appropriate reuse of dialyzers should be encouraged in low income countries like Pakistan, in order to prevent treatment dropouts due to costly therapy.

REFERENCES

1. Ahmed, S., Tariq, S., Chughtai, J., Saeed, F., Memon, S., & Alam, A. (2022). Vascular Calcification in maintenance Hemodialysis patients in Pakistan–A single center Cross-sectional study. Pakistan Journal of Kidney Diseases, 6(4), 16-25.
2. Abdul Razzaque, M. R., Tebha, S. S., Tukruna, A., Arif, A., Kogut, L. M., Afsar, N. A., ... & Zaidi, Z. A. (2023). 25-Hydroxyvitamin-D deficiency in chronic kidney disease stages III, IV, and V in South Asian population: a retrospective cohort. SAGE Open Medicine, 11, 20503121221148613.
3. Alostaz, M., Correa, S., Lundy, G. S., Waikar, S. S., & Mc Causland, F. R. (2023). Time of hemodialysis and risk of intradialytic hypotension and intradialytic hypertension in maintenance hemodialysis. Journal of Human Hypertension, 1-11.
4. El-Mashad, G. M., Omar, Z. A., & Seif, E. S. (2019). Evaluation of dialysis practice patterns in children having end-stage renal disease on maintenance hemodialysis at a pediatric nephrology unit. Saudi Journal of Kidney Diseases and Transplantation, 30(3), 615.
5. Hamid, A., Dhrolia, M. F., Imtiaz, S., Quereshi, R., & Ahmad, A. (2019). Comparison of adequacy of dialysis between single-use and reuse hemodialyzers in patients on maintenance hemodialysis. J Coll Physicians Surg Pak, 29(8), 720-3.
6. Kulkarni, M. J., Jamale, T., Hase, N. K., Jagdish, P. K., Keskar, V., Patil, H., ... & Patil, C. (2015). A cross-sectional study of dialysis practice-patterns in patients with chronic kidney disease on maintenance hemodialysis. Saudi Journal of Kidney Diseases and Transplantation, 26(5), 1050.
7. Coyne, D. W., Singh, A. K., Lopes, R. D., Bailey, C. K., DiMino, T. L., Huang, C., ... & Wanner, C. (2022). Three times weekly dosing of daprodustat versus conventional epoetin for treatment of anemia in hemodialysis patients: ASCEND-TD: a phase 3 randomized, double-blind, noninferiority trial. Clinical Journal of the American Society of Nephrology, 17(9), 1325-1336.
8. Abdelaal, A. A., & Abdelnabi, A. M. (2021). Study of Red Blood Cell Indices and Biochemical Parameters of Mineral Bone Disorders in Hemodialysis Patients. The Egyptian Journal of Hospital Medicine, 84(1), 1765-1771.
9. Ito, K., Ookawara, S., Hibino, Y., Imai, S., Fueki, M., Bandai, Y., ... & Morishita, Y. (2020). Skeletal muscle mass index is positively associated with bone mineral density in hemodialysis patients. Frontiers in Medicine, 7, 187.
10. Cheng, C. Y., & Kuo, Y. J. (2022). Single-centre cross-sectional study on the impact of cumulative erythropoietin on bone mineral density in maintenance dialysis patients. BMJ open, 12(4), e056390.
11. Ogawa, C., Tsuchiya, K., Tomosugi, N., & Maeda, K. (2020). A hypoxia-inducible factor stabilizer improves hematopoiesis and iron metabolism early after administration to treat anemia in hemodialysis patients. International Journal of Molecular Sciences, 21(19), 7153.
12. Sany, D., El Shahawi, Y., & Taha, J. (2020). Diagnosis of iron deficiency in hemodialysis patients: usefulness of measuring reticulocyte hemoglobin equivalent. Saudi Journal of Kidney Diseases and Transplantation, 31(6), 1263.
13. Correa, S., Scovner, K. M., Tumlin, J. A., Roy-Chaudhury, P., Koplan, B. A., Costea, A. I., ... & Investigators, M. (2021). Electrolyte Changes in Contemporary Hemodialysis: A Secondary Analysis of the Monitoring in Dialysis Study. Kidney360, 2(4), 695.
14. Pirklbauer, M. (2020). Hemodialysis treatment in patients with severe electrolyte disorders: Management of hyperkalemia and hyponatremia. Hemodialysis International, 24(3), 282-289.
15. Ságová, M., Wojke, R., Maierhofer, A., Gross, M., Canaud, B., & Gauly, A. (2019). Automated individualization of dialysate sodium concentration reduces intradialytic plasma sodium changes in hemodialysis. Artificial organs, 43(10), 1002-1013.
16. Yu, Y., Diao, Z., Wang, Y., Zhou, P., Ding, R., & Liu, W. (2020). Hemodialysis patients with low serum parathyroid hormone levels have a poorer prognosis than those with secondary hyperparathyroidism. Therapeutic advances in endocrinology and metabolism, 11, 2042018820958322.
17. Yamamoto, J., Nakazawa, D., Nishio, S., Ishikawa, Y., Makita, M., Kusunoki, Y., ... & Atsumi, T. (2020). Impact of weekly teriparatide on the bone and mineral metabolism in hemodialysis patients with relatively low serum parathyroid hormone: a pilot study. Therapeutic Apheresis and Dialysis, 24(2), 146-153.
18. Janjua, T. K., Mukhtar, K. N., Naveed, A. K., Ahmed, E. B., & Rehan, M. (2019). Frequency of maintenance hemodialysis patients meeting K/DOQI criteria for serum calcium, phosphorus, calcium phosphorus product and PTH levels; a single institutional experience from Pakistan: a cross sectional study. The Pan African Medical Journal, 33.
19. Anees, M., Ahmad, S., Raja, K. M., Mushtaq, M., & Ibrahim, M. (2020). Anemia and Mineral Bone Disorders in Patients with End Stage Renal Disease on Maintenance Hemodialysis. Pakistan Journal of Kidney Diseases, 4(1), 209-213.
20. Fabrizi, F., Cerutti, R., & Messa, P. (2021). Updated evidence on the epidemiology of hepatitis C virus in hemodialysis. Pathogens, 10(9), 1149.