Haematological profile of Chronic Kidney Disease Stage 5 patients undergoing maintenance Hemodialysis at a tertiary care centre.

Madhura AR[1], Jayaraj PM[2]

[1]Department of General Medicine, Mother hospital, Thrissur, Kerala, India

[2] Department of Nephrology, Mother Hospital, Thrissur, Kerala, India

Abstract

Background: Kidneys play a central role in the regulation of body fluids, electrolytes and acid- base balance. With progressive loss of kidney function, derangements in electrolytes and acid-base inevitably occur and contribute to poor patient outcomes. Timely intervention and effective management will minimize complications and can potentially be lifesaving.

Aim: To study the haematological profile in patients of chronic kidney disease (CKD) Stage 5 undergoing haemodialysis and to correlate the relation if any, between the study parameters.

Material and Methods: Study was conducted on 60 patients undergoing hemodialysis thrice a week. Complete hemogram, RFT, LFT, serum sodium, potassium, calcium and phosphorus values were obtained and their associations were statistically analysed.

Results: Out of 60 patients studied, 20% (n=12) had hemoglobin values <8 g/dl, 36% (n=36) had 8-10 g/dl and 12% (n=12) had ≥10 g/dl. 18% (n=11) had mild hyponatremia (130-135 mEq/L), 38% (n=23) had moderate (125-129 mEq/L) and 44% (n=26) had severe (<125 mEq/L) hyponatremia.80% of the study group (n=48) had serum calcium <9 mg/dl and 20% (n=12) had >9 mg/dl. 68% (n=41) of the patients had serum phosphorus >5.5 mg/dl and 32% (n=19) of them had <5.5 mg/dl. There was a significant positive correlation of serum sodium with serum calcium (r=0.752, p=0.0001), serum albumin (p=0.0001), hemoglobin (p=0.0001) and significant negative correlation with serum phosphorus (r=-0.730, p=0.0001), serum uric acid (p=0.003).

Conclusion: Anemia, hyponatremia, hyperkalemia, hypocalcemia and hyperphosphatemia are most commonly seen in hemodialysis patients. Appropriate timely intervention can significantly prevent the long-term morbidity in such patients.

Key words: CKD Stage 5, Maintenance hemodialysis, Anemia, Dyselectrolytemia

Introduction

Chronic kidney disease (CKD) encompasses a spectrum of patho-physiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate[11]. It has become a global epidemic with an estimated prevalence of 14% in the United States and 5- 15% throughout the world[2]. As the kidneys play a central role in the regulation of body fluids, electrolytes and acid- base balance, CKD and ESRD (End stage renal disease) predictably result in multiple derangements which, in turn, lead to serious complications.

Anemia occurs in 42%, 54% and 76% of CKD Stage 3, 4 and 5 patients, respectively, and is more severe in diabetics [3]. Anemia multiplies the mortality risks of diabetes, heart failure, and CKD. The primary reason for anemia in CKD is an absolute or relative deficiency of renal erythropoietin (EPO) synthesis. Individual sensitivity and responsiveness to Erythropoiesis-stimulating agents (ESA) are highly variable and dosing requirements are heterogeneous. Occult causes of blood loss, iron deficiency, vitamin deficiencies (B12 and folate), and inflammatory causes of ESA resistance should be ruled out secondarily. Inflammation upregulates hepcidin, a liver-synthesized protein that reduces gut iron absorption and impedes iron release from the

Corresponding Author:

Dr Madhura A R

Department of General Medicine, Mother Hospital, Thrissur, India

Email:madhura140@gmail.com

reticuloendothelial system to the developing erythron.

Hyponatremia (Na <135 mmol/l) is the most common electrolyte disorder in ESRD patients, ranging from 5 to 30%[4,5]. In dialysis patients, hyponatremia is mostly dilutional, due to excess water or hypotonic fluid intake. The risk factors being, malnutrition (hypalbuminemia), lower residual renal function and estimated GFR, co-morbidities and infection[6-8].

Potassium is eliminated mainly through the kidneys (90%) in about 6-12 hours and only a small amount (10%) through the colon. Dialysis patients are at high risk of developing hyperkalemia which can be caused or exacerbated by, (1) trans-cellular shift due to insulin deficiency, mineral metabolic acidosis and tissue breakdown (hemolysis, rhabdomyolysis, tumor lysis, and tissue ischemia), (2) high K+ intake and (3) medication-induced defects in renal K+ excretion, most commonly angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), mineralocorticoid receptor antagonists, K^+ sparing diuretics, and calcineurin inhibitors [9]. Also, Secondary hyperparathyroidism accompanying ESRD decreases K+ entry inside the cell through increased intracellular Ca2+, which suppresses the oxidative metabolism and the cellular ATP production and reduces the Na+- K+- ATPase activity[10].

Bone mineral metabolism and calcium-phosphorus homeostasis involve a complex interplay among kidneys, gut, bone and parathyroid glands. Hyperphosphatemia is seen in one-third to one-half of dialysis patients. The reasons include: increased dietary intake, insufficient removal during dialysis and most importantly, treatment-related issues like administration of high doses of calcitriol, or its analogues, which are known to enhance active phosphate absorption from the small intestine. The other factor is the lowering of intestinal free phosphate concentration, whether by dietary phosphate restriction or with phosphate binders, which is a known stimulus to enhance phosphate absorption from the small bowel[11,12]. Altered mineral metabolism manifests as secondary hyperparathyroidism due to reduced synthesis of 1,25-dihydroxyvitamin D in the kidney, which stimulates parathyroid hormone secretion directly and also indirectly through decreased intestinal absorption of calcium. In addition, there is reduced mobilization of calcium from bone due to decreased sensitivity of bone to PTH in conjunction with calcitriol deficiency. This results in hypocalcemia in advanced CKD.

Objectives:

Our objective is to study the haematological profile in CKD Stage 5 patients undergoing maintenance HD and correlate the association between different study parameters.

Material and Methods:

This was a cross-sectional observational study of 60 patients with ESRD undergoing maintenance hemodialysis (HD) thrice a week. Written and informed consent was taken from all the participants and their clinical and haematological data were collected. Patients included were older than 18 years diagnosed to have ESRD of varied aetiology undergoing maintenance HD thrice weekly in our dialysis unit. Complete hemogram, ESR, CRP, RFT, LFT, Serum sodium, potassium, uric acid, calcium and phosphorus, urine microscopy were done for all patients.

Statistical Analysis:

The study data was coded and entered in Microsoft Excel of windows 10 and analysed using the statistical software SPSS version 23. Results on continuous measurements are presented in Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. p-value <0.05 is taken as significant. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups. Pearson correlation co-efficient has been used to establish correlation between the variables. Unpaired t test, ANOVA and Post hoc ANOVA are used wherever found appropriate. Classification of Correlation Co-efficient (r): 0.1-0.3 = Small correlation, 0.3-0.5 = Moderate correlation, 0.5-0.7= Large correlation, 0.7-0.9=Very large correlation, 0.9-1.0=Nearly perfect correlation and 1=Perfect correlation. Significant figures: p-value ≤ 0.01=Strongly significant, 0.01-0.05=Moderately significant and 0.05-0.10=Suggestive significance.

Results

Sixty (n=60) patients with CKD Stage 5 undergoing maintenance hemodialysis were studied.

Table 1: Demographics of the study population

Age	Range 42-70 years	Mean age 59.3 years
Sex	Males	Females
	36 (60%)	24 (40%)
	Yes (Percentage)	No (Percentage)
Smoking	27 (45%)	33 (55%)
Alcoholism	21 (35%)	39 (65%)
Diabetes mellitus	42 (70%)	18 (30%)
Hypertension	60 (100%)	0

Their age range was between 42-70 years with a mean age of 59.3 years. 60% (n=36) were males and 40% (n=24) were females. 45%(n=27) of the study population were smokers and 35% (n=21) were alcoholics, 70% (n=42) had diabetes and all 100% (n=60) had hypertension (Table 1).

Table 2: Distribution of patients based on Hemoglobin

Hemoglobin (g/dl)	Number of patients (n=60)	Percentage (%)
<8	12	20
8-10	36	60
>10	12	20

Hemoglobin values ranged from 7.2 g/dl to 12 g/dl with a mean of 8.9±1.3 g/dl. 20% (n=12) of the study population had hemoglobin values <8 g/dl, 36% (n=36) had 8-10 g/dl and 12% (n=12) had ≥10 g/dl (Table 2).

Table 3: Distribution of patients based on Serum albumin

S. albumin (g/dl)	Number of patients (n=60)	Percentage (%)
<3	22	37
>3	38	63

Serum albumin levels of the study population ranged between 2.2 g/dl to 3.9 g/dl with a mean of 3.1±0.4 g/dl. 37% (n=22) of the participants had serum albumin <3 g/dl and 63% (n=38) had >3 g/dl (Table 3).

Table 4: Haematological profile distribution in the study population

	RANGE	MEAN ± SD
Hemoglobin (g/dl)	7.2-12	8.9±1.3
Serum albumin (g/dl)	2.2-3.9	3.1±0.4
Blood urea (mg/dl)	65-213	132.4±40.1
Serum creatinine (mg/dl)	6.6-14.5	9.6 ±1.8
Serum uric acid (mg/dl)	5.6-10.2	8.3±1.1
Serum sodium (mEq/L)	121-133	126±3.6
Serum potassium (mEq/L)	4.5-5.8	5.3±0.4
Serum calcium (mg/dl)	7-9.5	8.3±0.7
Serum phosphorus (mg/dl)	4.5-6.7	5.7±0.4

The blood urea values ranged from 65 mg/dl to 213 mg/dl with a mean of 132.4±40.1 mg/dl. The serum creatinine values of the study group ranged from 6.6 mg/dl to 14.5 mg/dl with a mean of 9.6±1.8 mg/dl. The uric acid levels ranged from 5.6 mg/dl to 10.2 mg/dl with a mean of 8.3±1.1 mg/dl (Table 4).

Table 5: Distribution of patients based on Serum sodium

S. sodium (mEq/L)	Number of patients (n=60)	Percentage (%)
130-135	11	18
125-129	23	38
<125	26	44

Serum sodium of the study participants ranged between 121 mEq/L to 133 mEq/L with a mean of 126±3.6 mEq/L. Out of 60, 18% (n=11) had mild (130-135 mEq/L), 38% (n=23) had moderate (125-129 mEq/L) and 44% (n=26) had severe (<125 mEq/L) hyponatremia (Table 5).

Table 6: Distribution of patients based on Serum calcium

Serum calcium (mg/dl)	Number of patients (n=60)	Percentage (%)
<9	48	80
>9	12	20

Serum potassium levels ranged between 4.5-5.8 mEq/L with a mean of 5.3±0.4 mEq/L (Table 4). Hyperkalemia of >5.5 mEq/L was present in 40% (n=24) of the study population. Albumin corrected serum calcium levels ranged from 7-9.5 mg/dl with a mean of 8.3±0.7 mg/dl. 80% of the study group (n=48) had serum calcium <9 mg/dl and 20% (n=12) had >9 mg/dl (Table 6).

Table 7: Distribution of patients based on serum phosphorus

Serum phosphorus (mg/dl)	Number of patients (n=60)	Percentage (%)
<5.5	19	32
>5.5	41	68

Serum phosphorus of the participants ranged between 4.5-6.7 mg/dl with a mean of 5.7±0.4 mg/dl. 68% (n=41) of them had serum phosphorus >5.5 mg/dl and 32% (n=19) of them had serum phosphorus <5.5 mg/dl (Table 7).

Table 8: Association between serum sodium and other haematological study parameters

	Hyponatremia	Number	Mean	Std. Deviation	p-value ANOVA
Hb (g/dl)	Severe	26	7.950	0.6088	0.0001
	Moderate	23	9.322	1.0488	
	Mild	11	10.382	0.9631	
	Total	60	8.922	1.2651	
Albumin (g/dl)	Severe	26	2.785	0.2130	0.0001
	Moderate	23	3.243	0.2711	
	Mild	11	3.582	0.2316	
	Total	60	3.107	0.3883	
Uric acid (mg/dl)	Severe	26	8.769	0.9346	0.003
	Moderate	23	8.196	0.9023	
	Mild	11	7.536	1.2160	
	Total	60	8.323	1.0647	
Urea (mg/dl)	Severe	26	142.038	34.3552	0.065
	Moderate	23	132.870	43.0816	
	Mild	11	108.545	40.0009	
	Total	60	132.383	40.1312	
Creatinine (mg/dl)	Severe	26	9.973	1.4421	0.152
	Moderate	23	9.596	1.9646	
	Mild	11	8.691	2.2170	
	Total	60	9.593	1.8354	
Calcium (mg/dl)	Severe	26	7.773	0.4201	0.0001
	Moderate	23	8.557	0.5663	
	Mild	11	9.136	0.2541	
	Total	60	8.323	0.6951	
Phosphorus (mg/dl)	Severe	26	5.981	.2466	0.0001

There was a significant positive correlation of serum sodium with serum calcium (r=0.752, p=0.0001), serum albumin (p=0.0001), hemoglobin (p=0.0001) and significant negative correlation with serum phosphorus (r=-0.730, p=0.0001), serum uric acid (p=0.003). However, there was no significant correlation of serum sodium with serum urea (p=0.065) and serum creatinine (p=0.152) (Table 8).

Discussion

The kidney plays an important role in maintaining the fluid, electrolyte and acid-base balance. The progressive loss of renal function causes dyselectrolytemia which occurs through mechanisms related to the chronic kidney disease and/or to the dialysis therapy and for this group of patients, it is associated with an increase in morbidity and mortality.

In our study, haematological profile of 60 ESRD patients undergoing hemodialysis was analysed. Their mean hemoglobin was 8.9±1.3 g/dl, mean serum urea 132.4±40.1 mg/dl, mean serum creatinine 9.6±1.8 mg/dl, mean serum uric acid 8.3±1.1 mg/dl, mean serum albumin 3.1±0.4 mg/dl, mean serum sodium 126±3.6 mEq/L, mean serum potassium 5.3±0.4 mEq/L, mean serum corrected calcium 8.3±0.7 mg/dl and mean phosphorus was 5.7±0.4 mg/dl (Table 4). There was a significant positive correlation of serum sodium with serum calcium, serum albumin and hemoglobin whereas, significant negative correlation of serum sodium with serum phosphorus and serum uric acid. Serum iron profile was measured in about 35 patients whose average serum iron levels were 55.86 µg/dl, average Total Iron Binding Capacity (TIBC) was 279.74 µg/dl and average serum transferrin saturation was 16%.

Seon Baek et al[13], studied 599 hemodialysis patients of mean age 76.3 years. Our study results were comparable to this study. The mean hemoglobin of study population was 9.4 ± 1.6 g/dl, mean creatinine 6.30 ± 2.50 mg/dl, mean albumin 3.27 ± 0.62 g/dl, mean sodium 137.3 mEq/L, mean corrected calcium

8.28 ± 0.84 mg/dl, mean phosphorus 5.00 ± 1.65 mg/dl. At the 90-day follow-up, 55 (28.8%) patients in the hyponatremia group, 51 patients (12.5%) in the normonatremia group had died. The 1-year overall mortality rates for patients with ESRD were 44.0% (84 out of 191 patients) in the hyponatremia group, 22.1% (90 out of 408 patients) in the normonatremia group. The study demonstrated a significant positive correlation of serum sodium with serum albumin (p<0.001) and significant negative correlation with serum phosphorus (p<0.001).

Nigwekar et al [6], studied hemodialysis patients from the Accelerated Mortality on Renal Replacement (ArMORR) cohort and found their mean sodium to be 138.2±3.4 mEq/L. Mean serum bicarbonate and serum albumin levels were lower in hyponatremic patients. In patients with hypocalcemia, 54.1% had hyperparathyroidism (P < 0.001). The mineral bone abnormalities that were associated with hyponatremiawere significantly associated with 1-year mortality (P <0.001).

The DOPPS study [14], conducted a mortality risk study on dialysis patients in three phases from the year 1996 to 2007. Survival models identified categories with the lowest mortality risk for serum calcium (8.6 to 10.0 mg/dL), corrected calcium (7.6 to 9.5 mg/dL), phosphorus (3.6 to 5.0 mg/dL). The greatest risk of mortality was found for calcium or corrected calcium levels greater than 10.0 mg/dL, phosphorus levels greater than 7.0 mg/dL.

Afshar R et al [15], conducted a cross-sectional study on 100 CKD patients (54 hemodialyzed, 46 pre-dialyzed). The severity of anemia among hemodialyzed patients was mild (Hb > 10 g/dL) in 5%, moderate in 70% and severe (Hb< 7 g/dL) in 25%, while in pre-dialyzed was mild in 45% and moderate in 55%.

Our study had comparable results with the other large cohort studies demonstrating the percentage of study population with anemia, dyselectrolytemia and altered bone mineral metabolism in CKD Stage 5 patients undergoing hemodialysis. The study also established the strong correlation of serum sodium levels with anemia, hypocalcemia, hyperphosphatemia and hyperuricemia. The prevalence of iron deficiency highlights the need for iron replacement therapy along with Erythropoietin administration to improve anaemia in such patients. This insight throws light on predicting the morbidity and mortality risk in hemodialysis patients and helps in intensive management of the complications early in the course of illness.

Conclusion

Anemia and dyselectrolytemia are a group of dialysis complications with immediate and long-term effects, which increase the morbidity and mortality among hemodialysis patients. The haematological profile of the dialysis patients must be monitored, and the treatment must be individualized and initiated as early as possible.

References

1. *Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J. Harrison's principles of Internal Medicine. 20th ed. New York: McGraw-Hill; 2018.*
2. *De Nicola L, Zoccali C. Chronic kidney disease prevalence in the general population:heterogeneity and concerns. Nephrol DialTransplant 2016;31:331- 335.*
3. *Kopple J, Massry S, Kalantar-Zadeh, K. Nutritional management of renal disease. 3rd ed. Baltimore: Williams & Wilkins; 2012.*
4. *Holland-Bill L, et al. Hyponatremia andmortality risk: a Danish cohort study of acutely hospitalized patients. Eur J Endocrinol 2015;173:71-81.*
5. *Liamis G, et al. Electrolyte disorders in community subjects: prevalence and risk factors. Am J Med 2013;126:256- 263*
6. *Nigwekar SU, Wenger J, Thadhani R, Bhan I. Hyponatremia, mineral metabolism, and mortality in incident maintenance hemodialysis patients: a cohort study. Am J Kidney Dis 2013;62:755-762.*
7. *Hecking M, Karaboyas A, Saran R, et al. Predialysis serum sodium level, dialysate sodium, and mortality in maintenance hemodialysis patients: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis 2012;59:238-248.*
8. *Waikar SS, Curhan GC, Brunelli SM. Mortality associated with low serum sodium concentration in maintenance hemodialysis. Am J Med 2011;124:77-84.*
9. *Tsering Dhondup Qi Qian.Electrolyte and Acid- Base Disorders in Chronic Kidney Disease and End-Stage Kidney Failure. Blood Purif 2017;43:179- 188.*
10. *Martin RS, Panese S, Virginillo M, Gimenez M, Litardo M, Arrizurieta E et al. Increased secretion of potassium in the rectum of man with chronic renal failure. Am J Kidney Dis 1986;8:105-110.*
11. *Suki WN, Moore LW. Phosphorus Regulation in Chronic Kidney Disease. Methodist Debakey Cardiovasc J 2016;12(4 Suppl):6-9.*
12. *Moore LW, Nolte JV, Gaber AO, Suki WN. Association of dietaryphosphate and serum phosphorus concentration by levels of kidney function. Am J Clin Nutr 2015Aug;102(2):444-53.*
13. *Seon Ha Baek, Sejoong Kim, Ki Young Na, Suhnggwon Kimand Ho Jun Chin. Predialysis hyponatremia and mortality in elderly patients beginning to undergo hemodialysis. Korean J Intern Med 2018;33:970-979.*
14. *Tentori F, Blayney MJ, Albert JM, Gillespie BW, Kerr PG, Bommer J et al. Mortality risk for dialysis patients with different levels of serum calcium, phosphorus, and PTH: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis 2008Sep;52(3):519-30.*
15. *Afshar R, Sanavi S, Salimi J, Ahmadzadeh M. Hematological profile of chronic kidney disease (CKD) patients in Iran, in pre-dialysis stages and after initiation of hemodialysis. Saudi J Kidney Dis Transpl 2010 Mar;21(2):368-71.*
16. *Timofte D, Tanasescu MD, Balcangiu Stroescu AE, Balan DG, Tulin A, Stiru O, et al. Dyselectrolytemia management and implications in hemodialysis. Experimental and Therapeutic Medicine. 2021 Jan 1;21(1):1-1.*
17. *Sueta D, Tabata N, Tanaka M, Hanatani S, Arima Y, Sakamoto K et al. Associations between corrected serum calcium and phosphorus levels and outcome in dialysis patients in the Kumamoto Prefecture. Hemodial Int 2020 Apr;24(2):202-211.*

18. *Levitt H, Smith KG, Rosner MH. Variability in calcium, phosphorus, and parathyroid hormone in patients on hemodialysis. Hemodial Int 2009 Oct;13(4):518-25.*

19. *Ramirez JA, Emmett M, White MG, Fathi N, Santa Ana CA, Morawski SG, Fordtran JS. The absorption of dietary phosphorus and calcium in hemodialysis patients. Kidney international. 1986 Nov 1;30(5):753-9.*

Conflict of interest: Nil
Source of funding: Nil

Date received: February 3rd 2021
Date accepted: April 28th 2021