Anemia and Mineral Bone Disorders in Patients with End Stage Renal Disease on Maintenance Hemodialysis

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Abstract:

Objective: To observe the pattern of anemia and mineral bone disorders (MBD)in patients with End Stage Renal Disease (ESRD) on maintenance hemodialysis (MHD).

Study design: Cross sectional observational study.

Place and Duration of study: Nephrology Department, Mayo Hospital and Shalamar Hospital, Lahore from 1st January 2019 1st March 2019.

Methodology: Two hundred patients who were undergoing MHD for more than three months were included in the study. Patients with Acute Kidney Injury (AKI) were excluded from the study. Patient's demographic data, laboratory reports and dialysis record were noted in a predesigned proforma.

Results: Two hundred patients were included in study, 105(52.5%) were male and rest of them were female. Major cause of ESRD was Diabetes Mellitus 83 (41.5%) followed by Hypertension 80 (40%) and Nephrolithiasis 15 (7.5%). Most of the patients belonged to middle age group, poor socioeconomic class, lower level of education and were getting twice-weekly dialysis. Mean hemoglobin was 10.17±1.69 gm/L and most of the patients 137 (68.5%) were anemic with hemoglobin level less than 11gm/dl. Iron was adequate in 170 (85%) patients with transferrin saturation more than 20%. Hypocalcemia (<8.5mg/dl), hypophosphatemia and calcium phosphorus product was less than 55 in 138(69%), 42(21%), 175(87.5%) respectively. Intact PTH was less than 100 pg/ml in 16(8.0%) patients supporting adynamic bone disease according to KDOQI guidelines and rest of the patients 184(92%) were having Intact PTH more than 100 pg/ml.

Conclusion: In this study, most of the patients were anemic most probably due to low dose of EPO and inadequate dialysis. High turnover and mixed bone disorders were present in majority of the patients.

Key Words: *CKD, Factors, Haemodialysis, Anemia, Mineral Bone Disorders,*

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Introduction:

When patients develop End Stage Renal Disease (ESRD), life cannot be sustained without renal replacement therapy (RRT). There are two modalities of RRT, dialysis and kidney transplant. Dialysis improves certain metabolic derangements caused by kidney failure including uremia,

metabolic acidosis, hyperkalemia and volume overload. Other components of chronic kidney disease (CKD) like anemia and CKD mineral bone disease (CKD- MBD) need additional medical management in the form of iron replacement, erythropoietin (EPO) administration, calcium supplements, phosphate binders and active form of vitamin D3. Anemia in CKD is mostly normochromic and normocytic, and is due to decrease in erythropoietin (EPO) production, decrease erythrocyte survival, bone marrow inhibition by uremic toxins, and deficiency of folate, iron, and vitamin B12.[1,2] Anemia of CKD can be managed successfully by recombinant EPO.[3] Anemia and CKD- MBD are important predictor of morbidity and mortality.[4-6] There is paucity of data on these important aspects of CKD locally. This study was conducted to determine the pattern of these manifestation and factors affecting them.

Patients and Methodology:

This cross-sectional study was conducted at the hemodialysis unit of Shalimar Hospital and Mayo Hospital, Lahore. It was conducted from January 2019 to March 2019. All patients who were on maintenance hemodialysis (MHD) for more than three months were included in the study. Patients who were on hemodialysis for less than three months and patients with AKI were excluded from the study. Demographic data including gender, age, education level, monthly income, duration of dialysis was entered in a predesigned proforma. Blood samples were drawn and sent to the laboratory for hematological (Hemoglobin), Biochemical parameters (Serum Calcium, Corrected Calcium, Serum Phosphorous and Intact PTH, serum Iron, Serum TIBC, Ferritin) and viral markers. Normal and abnormal parameters of anemia and CKD-MBD were decided on the basis of Kidney Diseases Outcome Quality Initiative (KDIGO) guidelines.[7,8] Anemia was defined as hemoglobin less than 11gm/dl, adequate transferrin saturation more than 20%, low turnover bone disease with intact PTH less than 100(pg/mL).[8] Data analysis was carried out using SPSS version 14.0 for windows (IBM, USA). Descriptive analysis was expressed in the form of percentages for qualitative variables and $\overline{X} \pm SD$ used for quantitative variables. A P-value $\leq$ 0.05 was considered as statistically significant.

Results:

Two hundred patients undergoing regular MHD for more than three months were included in the study. Majority of the patients 107(53.5%) were in middle age group while mean age of the patients were 48.11±13.74 (mean age= 48.11$\pm$13.74 and median age 50 years) and majority were male 105 (52.5%) as shown in Table No.1. Most of the patients 146 (73%) were having low education level i.e. less than 10th grade and belonged to poor socio-economic class, 178 (89%) with monthly income of less than Rs. 30,000/- (about US$194) per month. Almost equal number of the patients were diabetic 83 (41.5%), hypertensive 80 (40.0%) and rest of them were having history of Nephrolithiasis, Chronic GN, connective tissue diseases. Majority of the patients 108 (54%) were on MHD for less than 18 months and were on twice weekly 155 (77.5%) MHD. Mean hemoglobin was 10.17±1.69 gm/L and most of the patients 137 (68.5%) were anemic with hemoglobin level less than 11gm/dl. Iron stores were adequate in 170 (85%) patients with transferin saturation more than 20%. Hypocalcemia (<8.5mg/dl), hypophosphatemia and calcium phosphorus product was less than 55 in 138(69%), 42(21%), 175(87.5%) respectively. Intact PTH was less than 100 pg/ml in 16(8.0%) patients supporting adynamic bone disease according to KDOQI guidelines and rest of the patients 184(92%) were having Intact PTH more than 100 pg/ml. Median i-PTH and range of i-PTH were 367.20pg/ml, 19-2185 pg/ml respectively.

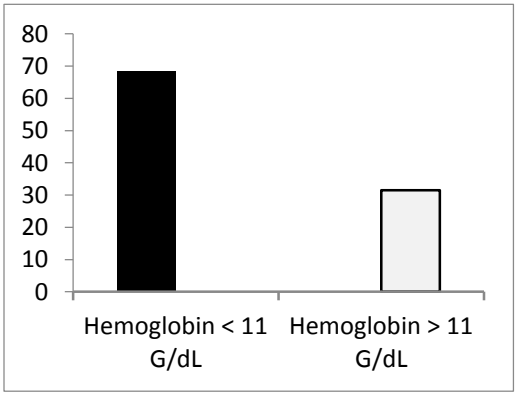
Table.No1. Laboratory data of 200 maintenance hemodialysis patients.

Sr. No	Laboratory Parameter	Mean± SD
1	Serum Hemoglobin (gm/dL)	10.17 ± 1.7
2	Serum Corrected Calcium (gm/dL)	8.15±1.02
3	Serum Phosphorus (gm/dL)	4.94±1.53
4	Calcium Phosphorus Product	41.29±16.04
5	Serum Albumin (gm/dL)	3.60±.42
6	Serum Na (mmol/L)	134.40±3.81
7	Serum K (mmol/L)	4.5645±.68
8	Serum Iron	115.27±67.48
9	TSAT (%)	34.74±15.56
10	Serum Ferritin	600.24±370.46
11	Serum TIBC	326.71±101.62
12	Serum Parathyroid (pg/mL)	412.73±295.72
13	Serum Urea (mg/dl)	147±52.95
14	Serum Creatinine(mg/dl)	6.92±3.41
15	HBsAg Positive Negative	31 (15.5%) 169 (84.5%)
16	AntiHCV Positive Negative	122 (61.0%) 78 (39%)

Discussion:

In this study mean age of the dialysis patients was much less as compared to international literature in which mean age of the dialysis patients is 60-65 years.[9] Similar pattern of patients having ESRD in younger age is reported in local literature.[10,11] This shows that patients are approaching end stage renal diseases at a younger age in this part of the world as compared to the developed countries. There may be many reasons for this discrepancy of age from the international literature. One reason is that the management of the CKD in its earlier stages is not up to the mark leading to advance complications at younger age and ESRD. Secondly, compliance of the patients towards the treatment and management is very poor. Due to the lack of health education patients usually don't take disease like diabetes and hypertension very seriously and avoid taking anti diabetic and anti-hypertensive medications regularly along with poor dietary compliance. Thirdly, poor socio-economic status further adds to the non-compliance to regular medications intake and routine follow-up with family physicians since majority of the health care system is dependent upon pay for service medical facilities.

Figure 1: Prevalence of Anemia of <11.0 G/dl in 200 regular maintenance hemodialysis patients.



In this study, major cause of ESRD was diabetes mellitus and hypertension which is similar to local and international studies but has changed since last decade locally when chronic GN was the leading cause of ESRD. [9,12,13] It may be due to better infection control measures that the prevalence of ESRD due to infectious GN has decreased and at the same time our dietary habits have changed leading to more metabolic syndrome and prevalence of Diabetes Mellitus.

Anemia is an important predictor of morbidity and mortality for the dialysis patients.[5] According to a local study, relative risk of mortality increases 1.58 times with every 1gm/dl decrease in hemoglobin level.[14] In this study most of the patients were anemic but mean hemoglobin level and number of the patients with anemia has improved as compared to previous prevalence of anemia in local literature.[15] It implies that there has been improvement in the management of the anemia in these patients in last couple of years. There are many causes of anemia in hemodialysis patients. Amongst these, EPO deficiency iron depletion, inadequate dialysis and hyperparathyroidism are the major reasons. In this study, iron stores were adequate (transferrin saturation more than 20%) in most of the patients (80%).

In fact, cost of Iron replacement is much less than erythropoietin administration. This corroborates into the fact that even with adequate iron replacement patients are anemic. Based on this observation other factors likely responsible for anemia are inadequate dialysis, inadequate dose of erythropoietin, infections and CKD-MBD. In this study, adequacy of hemodialysis is a factor affecting the anemia as most patients were getting 2/week HD. There is need to conduct further local studies for the correlation of adequacy of dialysis with anemia. We did not determine the dose EPO prescribed to the patients nevertheless, according to previous study, the average dose of EPO was 2652 IU/week.[14]

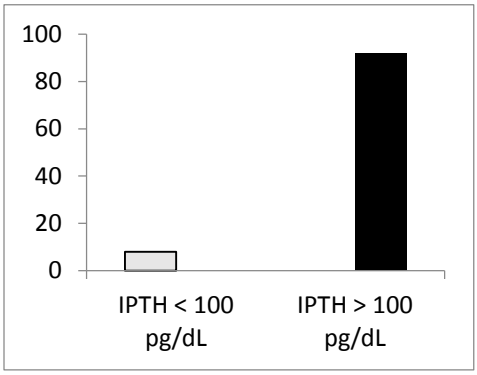


Figure 2: Prevalence of adynamic Bone Disease (i-PTH less 100 pg/dL) in 200 regular maintenance hemodialysis patients.

In this study, there was a high prevalence of Hepatitis C in hemodialysis patients as compared to Hepatitis B surface antigen positive patients. This high prevalence of Hepatitis C may be the reflection of high incidence of Hepatitis C in general Population. According to Arshad et al. prevalence of Anti HCV is 11.5% in general population in Pakistan.[16] A high rate of seroconversion of Hepatitis C during hemodialysis, which increases with the duration of hemodialysis and with the number of blood transfusion for maintaining hemoglobin. Along with that universal precautionary measures are not strictly followed by dialysis staff like wearing gloves and hand sanitization while moving from hepatitis C positive to hepatitis C negative patients. Although the international guidelines don't recommend isolation of Hepatitis C positive and negative patients but there is a need to develope local guidelines for the isolation of Hepatitis C positive patients from Hepatitis C negative patients.[16]

KDOQI guidelines has introduced the term CKD-MBD in an attempt to bring together alteration in mineral metabolism markers, renal osteodystrophy, and vascular or other soft tissue calcification.[8] CKD renal osteodystrophy is divided into low turnover, high turnover and mixed turnover bone disease. The gold standard diagnostic modality for this division is bone marrow biopsy, which is usually not possible due to non-availability, difficult to perform and interpretation. Clinical criteria based on i-PTH and alkaline phosphatase are usually used to decide this issue. In this study most of the patients had mixed or high turnover bone disease and mean i-PTH was much less (412.73±295.72) as compared to another international study in which

mean value was 607.74 ± 649.55 pg/ml.[17] This discrepancy may be due to over use of calcium phosphate binders and active form of Vitamin D3 at early stage of CKD by General and family physicians (personal experience). Hence, these patients present to Nephrologists with normal or over suppressed PTH levels.

In conclusion, among 200 dialysis patients undergoing MHD for more than 3 months majority had HCV, anemia and low prevalence of adynamic bone disease. Multicenter studies including a large population of patients should be studied at the time of presentation and after a defined follow-up period to better understand the patient population on MHD.

Conflict of Interest: None declared

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