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A Cross-Sectional Comparative Study of CKD-MBD in Peritoneal Dialysis Versus Hemodialysis Patients

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ABSTRACT

Objective:

- *To compare the demographic data of patients on PD versus HD*
- *To Carry out a comparative analysis of the important variables that are manifested in disturbances in mineral bone metabolism in CKD patients that are undergoing HD versus PD*

Methods: *Data was collected quantitatively. The groups were comparable with respect to underlying disease and demographic characteristics. The variables studied were, serum calcium levels, phosphorus levels, vitamin D levels, parathyroid hormone levels, serum albumin, hemoglobin levels and the urine output. It was also established whether the patients were on phosphate binders or not. The decline of residual renal function during dialysis and its relationship with mineral metabolism has been evaluated.*

Results: *The results of the study showed no difference in gender distribution in the two modalities. Majority of the patients on hemodialysis and peritoneal dialysis are above 35 years. The youngest patient – 11 years is on APD. 90% (n=43) of the total cases are on CAPD. 47% (n=22) are using 2.5% dianeal solutions. Majority of the PD patients 81% n= 39 did the bag exchange procedure themselves. The study revealed that Patients on PD are on dialysis longer with the longest patient being 18 years on PD. Patients on PD had higher hemoglobin levels. Patients on PD had better residue renal function since thy had bigger renal outputs. The highest level of parathyroid hormone levels was found in PD patients the highest being greater than 2000 pg/ml. Most patients accounting for 88% n=42 in HD and 75% n=36 in PD did not have IPTH checked. Majority of the patients in both PD and HD are not on phosphate binders accounting for 54 % n= 26 in HD and 71% n= 34 on PD. Vitamin D levels were highest in hemodialysis. Most patients accounting for 88% n=42 in HD and 79% n=38 did not have vitamin D levels checked. Majority of the patients on peritoneal dialysis had low albumin levels compared to hemodialysis. 8% of HD patients did not have albumin levels checked as compared to only 2% n=1 on PD. Patients on peritoneal dialysis have higher calcium levels. 10 % n=5 and 25% n= 12 of patients on PD and HD consecutively did not have phosphorous monitored. Patients on hemodialysis had higher phosphorous levels. Majority of patients on PD have diabetes -46% n=22 compared to 38% n= 18 on hemodialysis.*

Conclusions: *In conclusion, Majority of patients undergoing both peritoneal dialysis and hemodialysis have Hyperparathyroidism, hyperphosphatemia which is one of the indicators of mineral bone disease in CKD. The calcium levels were normal in most of the patients.*

Keywords

Chronic Kidney Disease, Mineral and Bone Disorder, CKD-MBD, Peritoneal Dialysis, Hemodialysis, Dialysis modalities.

Background

Chronic kidney disease-mineral bone disorder (CKD-MBD) previously called renal bone disease is a systemic disorder of

mineral and bone metabolism. Itoccurs when the kidneys fail to maintain the proper levels of calcium, phosphate, vitamin D and parathyroid hormone (PTH) in the blood. Calcium and vitamin D tend to be low, and phosphate and PTH high. CKD-MBD affects most patients with kidney failure: predialysis patients with CKD or those on dialysis. Transplant patients whose transplant is working well can control the problem, but it can worsen again if the transplant fails. CKD-MBD never goes away completely [1].

Adynamic Bone disease is a common complication in PD patients. PD patients have transperitoneal removal of Phosphates at a rate of approximately 200 to 300 mg per day, so it is difficult to maintain appropriate serum Phosphate levels using PD alone [2].

Main Objective

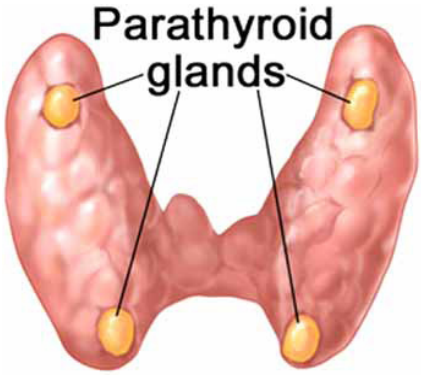
The main objective of our study was to evaluate monitoring of mineral born disease in PD versus HD patients.

Specfic Objectives

- To give a preview of mineral bone disease in CKD and ways of preventing it
- To compare the demographic data of patients on peritoneal dialysis (PD) versus hemodialysis (HD)
- To Carry out a comparative analysis of the important variables that are manifested in disturbances in mineral bone metabolism in CKD patients that are undergoing HD versus PD
- To establish trends in hemoglobin and serum albumin levels as well as urine output among patients undergoing HD versus PD
- To establish important data in dialysis patients such as the number of bag exchanges in PD, dialysate volumes used, who does the exchanges and the number of years the patients have been on dialysis

Literature Review

Parathyroid hormone (**PTH**) is a peptide hormone which is synthesized and produced in the 4 parathyroid glands which reside behind the thyroid gland in the anterior neck. The release of PTH is stimulated by low calcium in the blood.



PTH raises the blood calcium level by: breaking down the bone (where most of the body's calcium is stored) and causing calcium release. It also sends a signal to the kidneys to reabsorb calcium in the collecting system and excrete phosphorous. PTH increases the conversion of 25 hydroxy vitamin D to 125 dehydroxy vitamin D in the kidneys which stimulates the intestines to absorb calcium and phosphorous. Intact **PTH** (**iPTH**) is the biologically active form and is secreted when the calcium level is low. Active vitamin D hormone (1,25-dihydroxy vitamin D) regulates the uptake of calcium from the intestinal tract, the mineralization of the bones, the differentiation of osteoblasts and bone matrix synthesis. Even a slight vitamin D deficiency in the blood causes an increase in bone atrophy. hypovitaminosis D is a risk factor for autoimmune diseases (e.g. multiple sclerosis, Crohn's disease, type 1 diabetes mellitus), infectious diseases (e.g. infections of the respiratory tract, tuberculosis) and cardiovascular diseases. The 25-OH Vitamin D ELISA is designed for serological determination of vitamin D concentrations in the blood. The serum level of 25-OH vitamin D, which of all vitamin D metabolites in the blood stores most vitamin D, is a suitable indicator of the actual vitamin D supply in the body [3].

Pathophysiology of Chronic Kidney Disorder-Mineral Bone Disorder

CKD-MBD is a systemic disorder of mineral and bone metabolism. When the kidneys are not functioning, the production of 1,25 dihydroxycholecalciferol reduces quickly. This leads to hypocalcemia because less calcium is absorbed from the intestines. Renal excretion of phosphorous in addition is decreased Phosphorous levels thus increase in the body. The phosphorous retention again leads to hypocalcemia because phosphorous forms a complex with calcium c*P product. Hypocalcemia leads to an increase in parathyroid hormone production by the parathyroid glands. This is called secondary hyperparathyroidism. Disturbances in mineral bone metabolism is manifested as:

- Hyperphosphatemia
- Hypocalcemia
- Hyperparathyroidism

These are commonly observed in CKD.

Disorders of mineral metabolism such as plasma calcium, phosphorous, and intactparathyroid hormone contribute to the development of vascular calcification and cardiovascular calcification, cardiac ischemia increasing cardiovascular mortality [3].

Prevention of Hyperparathyroidism

K/DIQO guidelines recommend measuring of calcium. Phosphorous and iPTH on regular basis: Every month for calcium and phosphorous. iPTH should be monitored every 3 months. Serum level of corrected calcium should be between8.4 and 9.5 mg/dl (2.10 and 2.37mmol). Serum phosphorous should be between3.5 and 5.5mg/dl (1.13 and 1.78mmol). Ca*p product concentration should be maintained at less than55mg2/d12 (4.4mmol2/L2). The guidelines recommend a phosphate restricted diet, Phosphate binders. Calcium based phosphate binders are effective but can lead to undesirable levels of calcium. Aluminum based phosphate binders are good but they contain aluminum

that accumulate and lead to bone disease and encephalopathy. Sevelamer hydrochloride and lanthanum carbonate are free of aluminum and calcium. Next to phosphate binders, vitamin D is prescribed which causes suppression of PTH.

A disadvantage of vitamin D is that it causes an increase of plasma calcium and phosphorous concentration which can lead to hypercalcemia and more deposition of calcium phosphorous [4].

Methodology

A cohort of 2 groups of 48 patients each undergoing PD and HD was studied. This was a cross-sectional comparative study. Data was collected and analyzed quantitatively. The groups were comparable with respect to underlying disease and demographic characteristics. The study was carried out at Madras medical mission PD and HD outpatient departments. All patients on HD and PD were included in the study. Patients who had missing data, patients who had expired, Patients who had lost follow up were excluded from the study. 48 patients were sampled conveniently from the PD and the HD units. The variables studied were, serum calcium levels, phosphorus levels, vitamin D levels, parathyroid hormone levels, serum albumin, hemoglobin levels and the urine output. It was also established whether the patients were on phosphate binders or not. The decline of residual renal function during dialysis and its relationship with mineral metabolism has been evaluated. Other variables captured were the number of years on dialysis, the number of exchanges for PD patients, who does the exchange, whether on CAPD or PD and the dianeal solutions used. Other important baseline variables were studied. Data was collected conveniently from the files of patients undergoing HD and PD. The raw data was entered and coded in a computer software. Data was analysed using statistical package for the social sciences (SPSS) version 22.0. No names of the patients were revealed from the records. Only code numbers were used. Confidentiality was maintained and thus details were collected for no other purpose than for this study. Approvals were obtained from the head of the nephrology department where the study was carried out.

Results

Majority of the patients on HD and PD are above 35 years. The youngest patient – 11 years is on APD. There was no difference in gender distribution in the two modalities. This is shown in Table 1 below.

Table 1: Showing the Baseline characteristics.

Variable	PD (N=48)	HD (N=48)	P-Value
Mean age in years	55.65 ± 14.177	50.083 ± 14.925	0.074
Mean Vintage of dialysis in years	2.971 ± 3.493	1.764 ± 0.922	0.025
Mean Hemoglobin in g/L	10.379 ± 1.787	9.610 ± 1.778	0.037
Mean urine output in ml	499.50 ± 383.580	357.20 ± 318.794	0.142
Diabetes (%)	18.38 %-	22.46%	

Majority of the patients on PD accounting for 88% (n= 42) are on 2L volume exchanges. Majority of the patients on APD accounting for 72% [5] were on 10-hour therapy, Majority of the patients on CAPD accounting for 73% (n=30) carried out 3 bag exchanges per day, Majority of the patients accounting for 47% (n=22) are using 2.5% dianeal solutions, Majority of the patients accounting for 90% (n=43) of the total cases are on CAPD. All these have been summarized as shown in Table 2.

Variable	
PD Modality	90% -CAPD 10%-APD
Solutions used	47% (n=22) are using 2.5% dianeal solutions
Frequency of exchanges	73%- 3 exchanges 27%- 4 exchanges
APD Therapy	72% 10-hour therapy
Volume	88% (n= 42) are on 2L volume exchanges

Table 2: Showing PD details.

The highest level of parathyroid hormone levels was found in PD patients as shown below with **PD: 535.758 ± 516.757** versus **HD: 412.817 ± 238.914**. **Pvalue = 0.052.**

Table 3: Showing Summary of CKD MBD data.

	PD	HD	P-Value
PTH	535.758 ± 516.757	412.817 ± 238.914	0.052
P	4.821 ± 1.362	5.904 ± 1.740	0.000
Ca	8.640 ± 0.910	8.338 ± 0.843	0.000
Vitamin D	17.524 ± 11.844	24.800 ± 27.345	0.229

Discussion

The study revealed that CKD more commonly affects patients above 35 years. This is in line with Centers for Disease Control and Prevention- CKD Surveillance System—United States that shows CKD becomes more common with increasing age. After the age of 40, kidney filtration begins to fall by approximately 1% per year. In addition to the natural aging of the kidneys, many conditions that damage the kidneys are more common in older people including diabetes, hypertension, and heart diseases [5]. APD patients were fewer than CAPD patients. An economic analysis of CAPD and APD revealed that out of pocket was higher in APD than CAPD. Most of the CKD patients are not funded and they tend to choose CAPD [6]. Most of the patients use 2.5% because a higher dextrose concentration moves fluid and more wastes into the abdominal cavity, increasing both early and long-dwell exchange efficiency (National Institute of Diabetes and Digestive and Kidney Diseases). Majority of the patients had 3 bag exchanges. A typical prescription for CAPD requires three or four exchanges during the day and one long—usually 8 to 10 hours—overnight dwell time as the patient sleeps (NIDDK). Patients on APD were mainly on 10-hour therapy which is the recommended total therapy time. Time on cycler – 8 to 10 hrs. The longer the time the patient spends on the cycler the better the clearance [2]. Most of the patients were on 2litre volume exchanges since they were adults. 4 (number of exchanges) x 2L (dwell volumes) is the typical prescription. 4 x 2.5L in larger patients with small RRF or anuric patients who weigh >75 kg. 3 x 2L in smaller patients or in patients with good RRF [2].

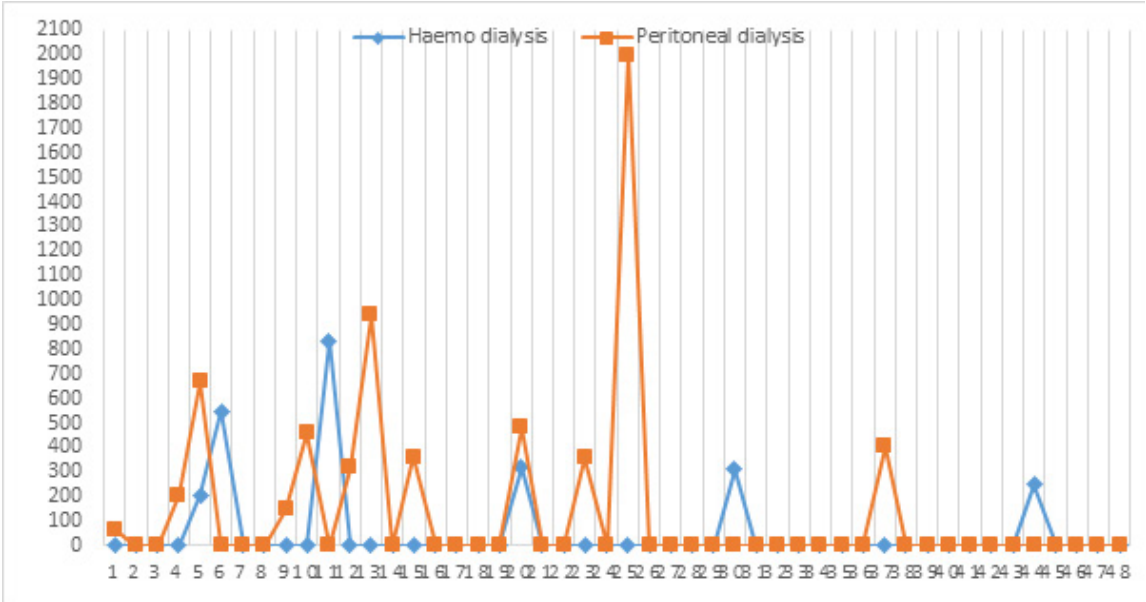


Figure 1: Showing the parathyroid hormone levels comparison data.

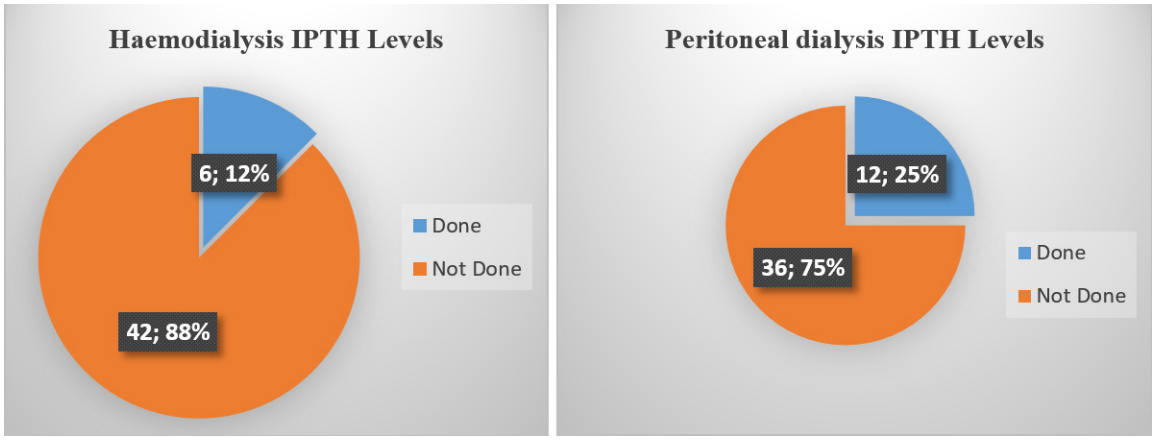


Figure 2: Showing IPTH monitoring in HD versus PD.

Majority of the patients in both PD and HD are not on phosphate binders accounting for 54 % n= 26 in HD and 71% n= 34 on PD as shown below

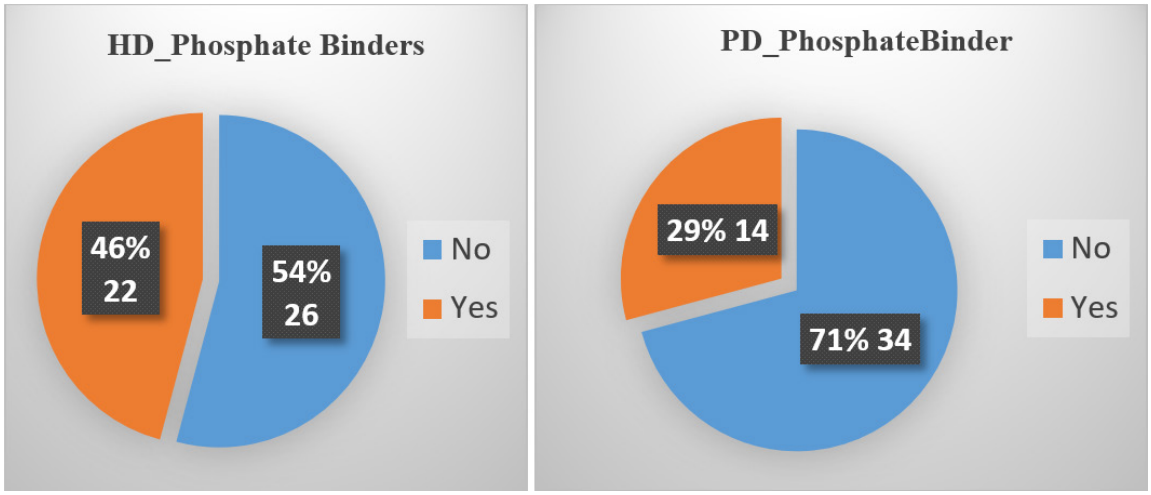


Figure 3: Showing comparison of use of phosphate binders in HD versus PD.

Mean value was found to be for PD: 17.524 ± 11.844 versus HD: 24.800 ± 27.345. P-value = 0.229

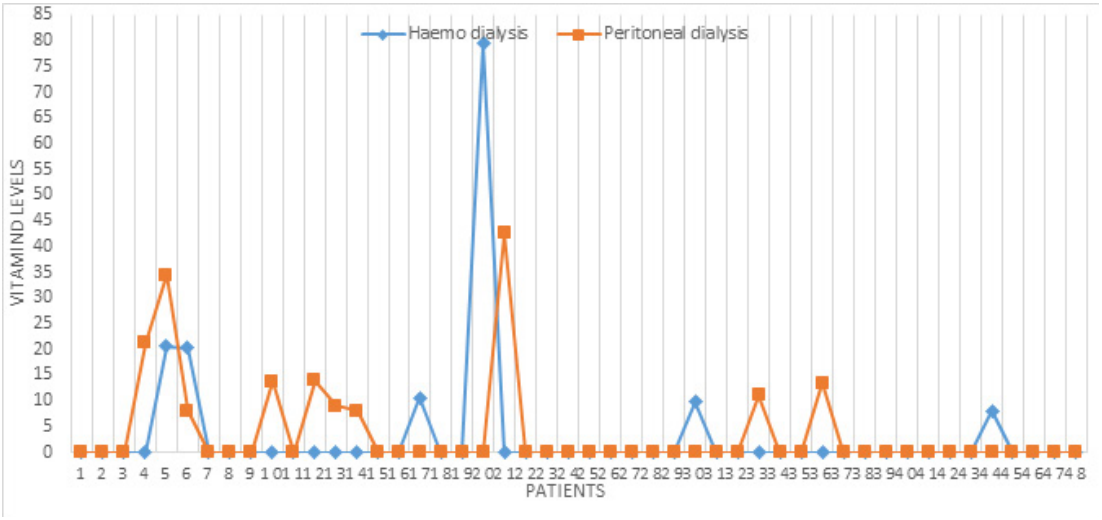


Figure 4: Vitamin D levels monitoring.

Most patients accounting for 88% n=42 in HD and 79% n=38 did not have vitamin D levels checked as per Figure 5 below

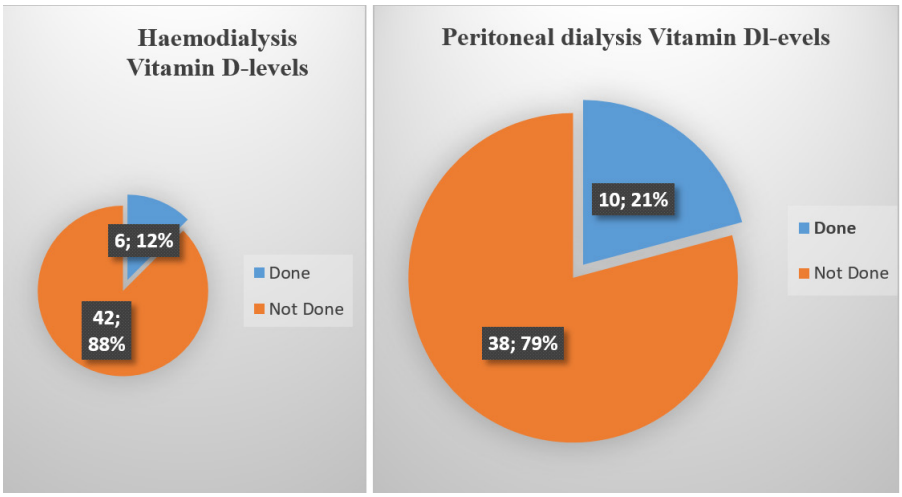


Figure 5: Showing vitamin D levels monitoring.

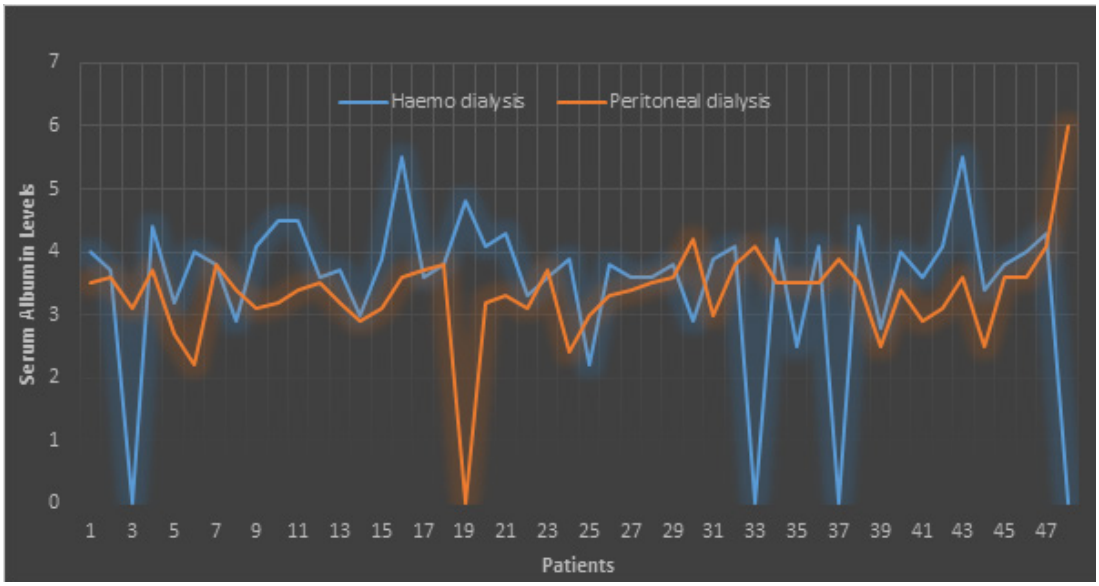


Figure 6: Showing comparison of serum albumin levels IN HD versus PD.

4.8% of HD patients did not have albumin levels checked as compared to only 1.2% n=1 on PD as shown in Figure 7 below

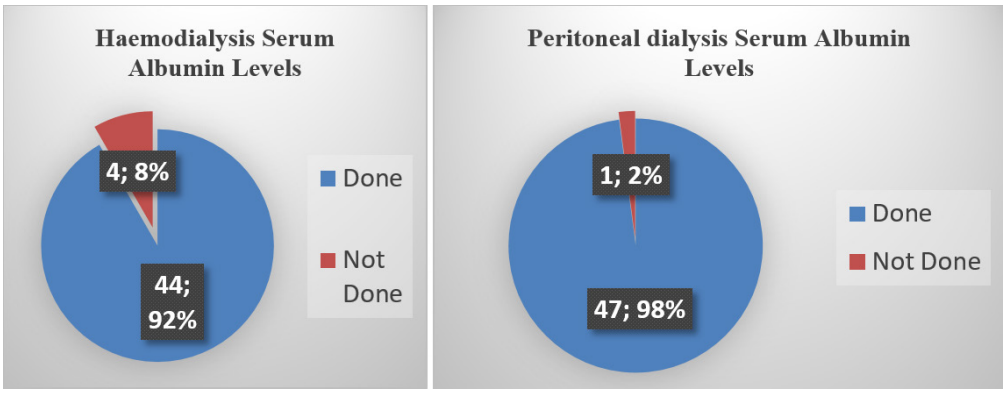


Figure 7: Comparison of serum albumin levels monitoring in HD versus PD.

Patients on PD had higher calcium levels as shown below. PD: 8.640 ± 0.910. HD: 8.338 ± 0.843. P-value = 0.000 as shown in Figure 8 below

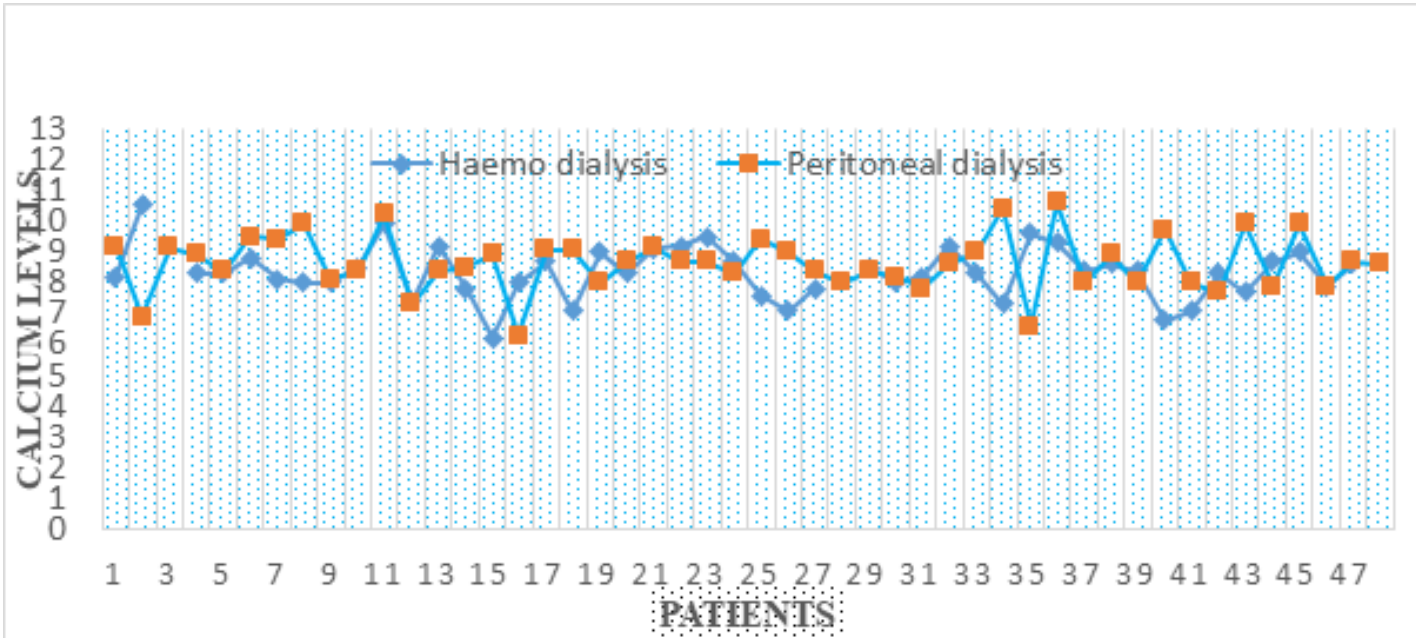


Figure 8: Showing calcium levels in haemodialysis versus PD.

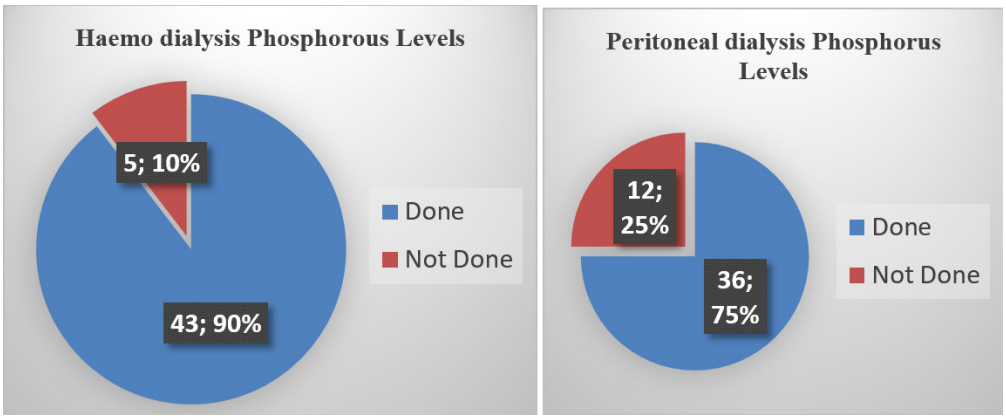


Figure 9: Comparison of phosphorous monitoring.

Patients on HD had higher phosphorous levels as per figure 10 shown below. **PD: 4.821 ± 1.362**. **HD: 5.904 ± 1.740**. **P-value = 0.000**

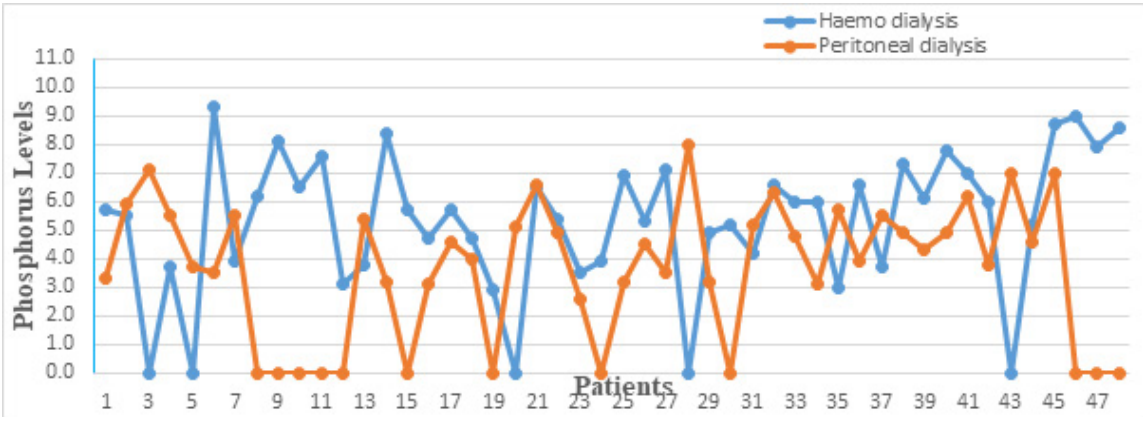


Figure 10: Comparison of phosphorous levels.

Figure 11: Showing persons performing PD.

Patients on PD had better renal residual function as shown in Figure 12 below

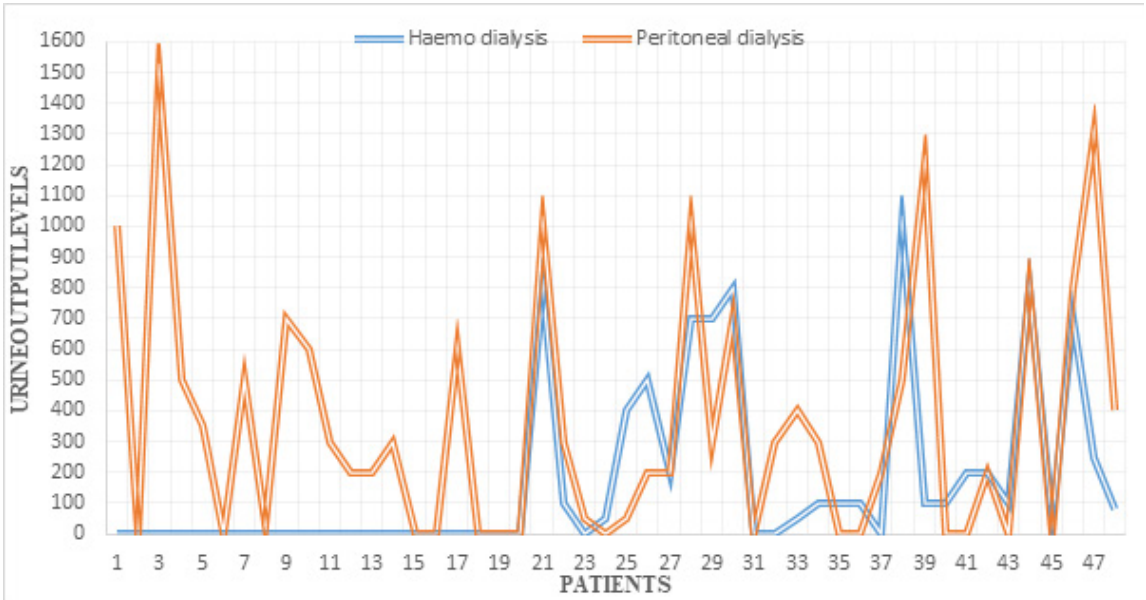


Figure 12: Showing urine output comparison in PD versus HD.

Patients on PD had higher hemoglobin levels as shown on Figure 13 below

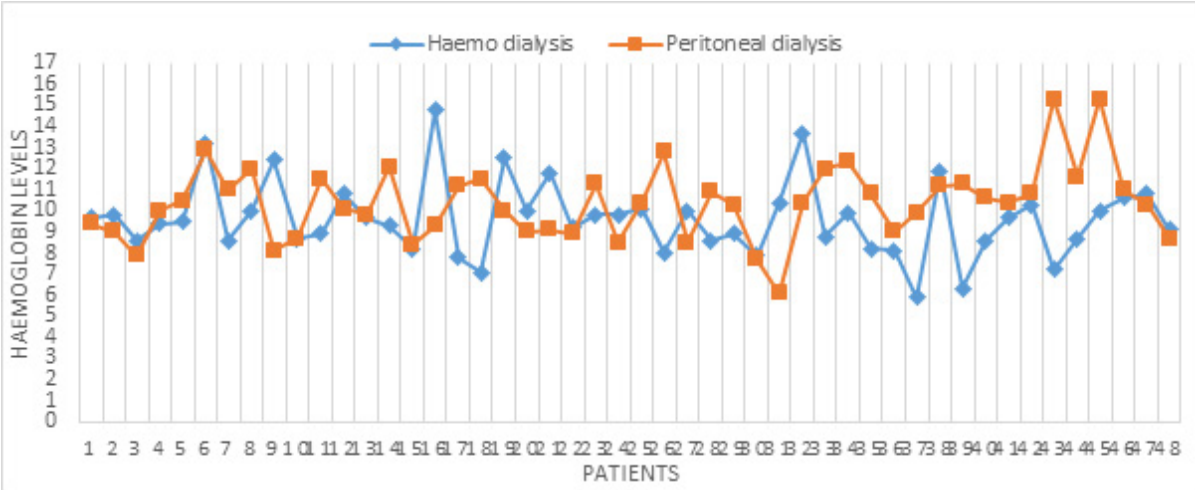


Figure 13: Comparison of hemoglobin levels of PD patients versus HD.

Patients on PD are on dialysis longer with the longest patient being 18 years as shown on Figure 14 below

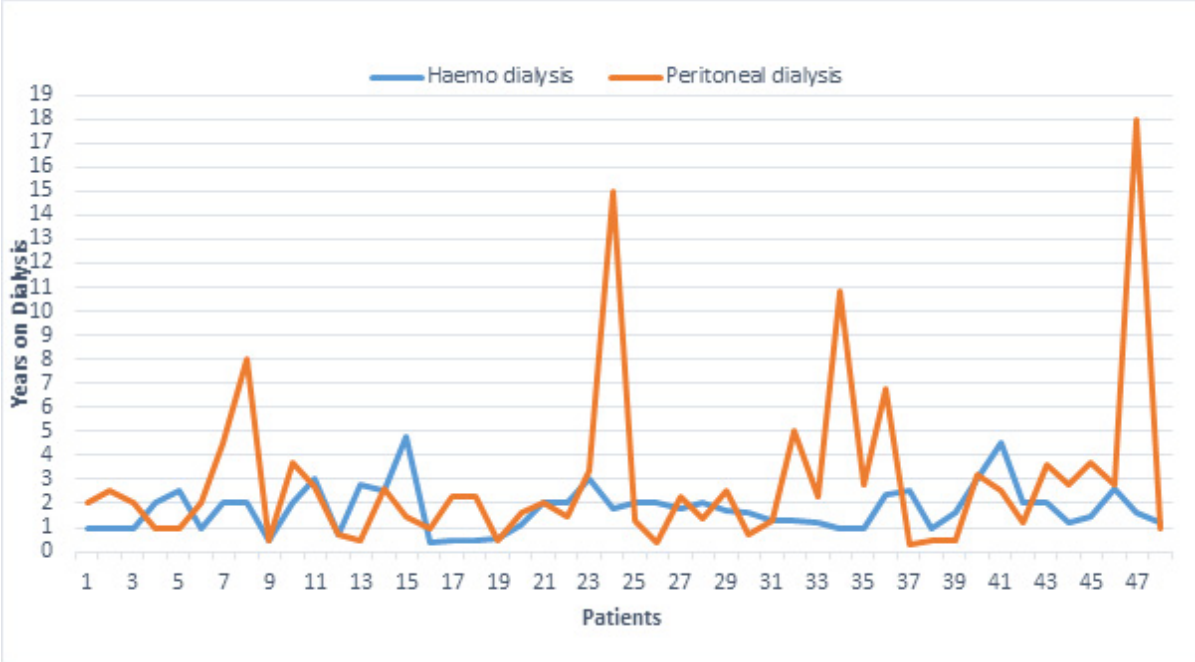


Figure 14: Comparison of the number years on HD versus PD.

Majority of patients on PD have diabetes -46% n=22 compared to 38% n= 18 on HD

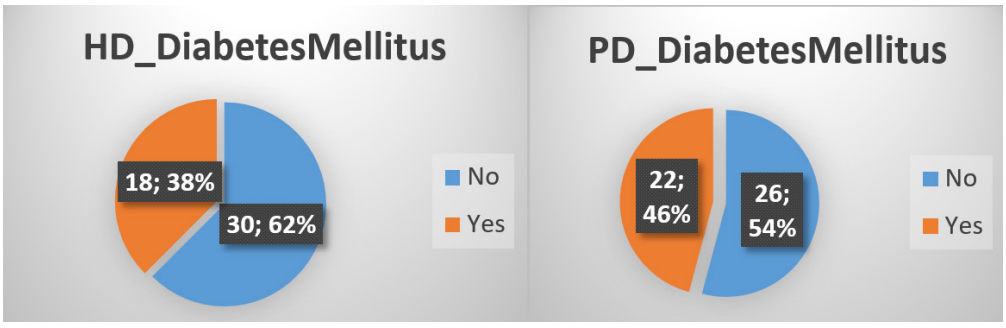


Figure 15: Showing comparison of diabetes in HD versus PD.

Problems of increasing dwell volumes- include back pain, abdominal distension and even shortness of breath. Increasing frequency of dwells is less effective than increased volumes for improvement of creatinine clearance as equilibration curve for creatinine is rising 4 hours after the dwell. It is also more expensive and may interfere with patient's lifestyle. A switch from 4x2l to 4x 2.5 l increases the Kt/V by 18 to 20%). Increasing tonicity of dialysis solution increases both ultrafiltration and clearance but may lead to hyperglycemia, hyperlipidemia, obesity and long-term peritoneal membrane damage [2].

The bag exchanges were performed by the patient himself. Patients on PD had reserved renal function which in line with other researchers who found out that many patients on PD will have preserved residual kidney function [7]. PD patients had more years on dialysis. PD Patients have 48% greater survival than HD [8]. In this study, PD patients had higher hemoglobin levels. Patients undergoing CAPD generally show higher hematocrits and lower transfusion dependencies than HD patients [9]. Studies show that Majority of the patients on PD had low albumin levels compared to HD [10]. It was found out that serum albumin in HD group was much more than that in PD group [10]. This study shows that Patients on PD had higher Urine output than HD. Residual kidney function (RKF) plays a crucial role in clearance of uremic toxins, prevents volume overload and its sequelae, such as left ventricular hypertrophy (LVH) and congestive heart failure (CHF), and is associated with improved metabolic parameters [11]. RKF is referred to as the "heart of PD" but very few studies have analyzed the relation between RKF and mortality and other important outcomes in HD patients. PD patients have a higher eGFR and higher calcium concentrations and lower phosphorous and ca*p product concentrations [3]. PD patients had a higher parathyroid hormone, higher calcium levels. Patients on HD had higher phosphorous levels. In patients undergoing PD, serum levels of calcium (Ca), phosphate (P), and parathyroid hormone (PTH) remain relatively constant, irrespective of the timing of treatment. This is because PD is a continuous blood purification procedure, and differs with HD, where the serum levels of these factors change following each dialysis session, and so pre-dialysis values are considered baseline values [12]. Majority of the patients in both PD and HD are not on phosphate binders and vitamin D analogues. HD Patients receiving some injectable vitamin D have shown to have survival advantage compared to those who did not [12].

Conclusion

Adynamic bone mineral disease was not significant compared to other researches. Majority of patients undergoing both peritoneal dialysis and hemodialysis have Hyperparathyroidism, hyperphosphatemia which is one of the indicators of mineral bone disease in CKD. The calcium levels were normal in most of the patients. Mineral metabolism in dialysis patients should be under tight control. Additional gastrointestinal elimination of phosphorous by phosphate binding agents is necessary in almost all patients to achieve a neutral phosphorous balance.

Recommendations

Mineral metabolism in dialysis patients should be under tight control. Additional gastrointestinal elimination of phosphorous by phosphate binding agents is necessary in almost all patients to achieve a neutral phosphorous balance Restriction of dietary Phosphate intake, conservation of residual kidney function for excretion of Phosphates, are recommended to maintain the blood Phosphate level in the appropriate range.

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