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HEMODIAFILTRATION IN IRAQI PATIENTS A COMPARATIVE STUDY

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Abstract
Background: Hemofiltration (HDF) seems to be the most effective technique in the field of renal function replacement by dialysis since it improves the general well-being of patients getting this medical procedure and cardiovascular wellness. It also raises the rate of recovery. It effectively manages hemoglobin by increasing erythropoietin levels, decreasing inflammation, and improving blood electrolyte composition.
The aim of study: assess the benefits and effect of HDF on biochemical parameters in chronic HD patients after 6 months of transferring to HDF.
Patients and methods: A retrospective study was conducted in the HDF unit at Baghdad Teaching Hospital, Medical City Complex in Baghdad from March 1, 2024, to October 1, 2024. We selected a convenience sample diagnosed with end-stage renal failure who were receiving continuous hemofiltration treatment according to specific criteria. The data were collected directly from patient records at the dialysis center and translated into a computerized database structure. Using the SPSS software version.
Results: the total sample were 58 patients with mean age of 55.03±14.81 years and more than third of the participants were male (71%). We compared the biochemical test of participants at the baseline and after 6 months from hemodiafiltration therapy. we found a decrease in the mean of blood urea, creatinine, Na and K level (46.09 mg/dL, 9.17 mg/dL, 137.22 and 5.3 mm/l respectively) .while the blood level of Ca, Hb and ferritin albumin ,PTH, increase after 6 months of HDF (8.981 mg/dl, 10.42mg/dl, 682.98, 299.36 mg/dL and 4.017ng/ml respectively)
Conclusion: Hemodiafiltration significantly increases some biochemical parameters (hemoglobin and calcium) while significantly decreasing others. (Na, K and urea).
Keywords: Hemodiafiltration (HDF), End-stage renal disease (ESRD), Biochemical parameters, Erythropoietin alfa (EPO), Maintenance dialysis therapy

Introduction

Hemodialysis (HD) remains the predominant form of renal replacement therapy (RRT) worldwide, with variations in access to healthcare and choice of RRT often determined by the economic resources of different nations [1–4]. Patient engagement in choosing an RRT method, supported by thorough information sharing, enhances satisfaction and compliance, underscoring the value of shared decision-making in treatment planning [5–8]. New research continually informs HD practices, as efforts are made to improve survival rates, reduce complications, and elevate the quality of life for patients with end-stage kidney disease (ESKD) [9–11]. Despite technical advances in HD delivery, mortality among HD patients is still

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significantly higher than that of the general population, creating a sustained impetus for improved care [12–14]. In the 1980s, HD technology relied on acetate dialysate, machines without precise volumetric control, and low-flow, low-flux dialyzers [15]. By the 1990s, advances led to the adoption of bicarbonate dialysate, better ultrafiltration control, higher blood flow rates, and high-flux dialyzers [16]. This evolution continued with the development of online hemodiafiltration (HDF) techniques, allowing for the use of dialysate as a replacement fluid and marking a substantial improvement in dialysis technology [17].

The recent interest in high-convection-volume HDF, which is thought to better mimic natural kidney function, raises the question of whether it could become a standard for chronic HD patients [18]. Defined in 2013 by the European Convective Working Group, HDF involves high-flux dialyzers and a minimum effective convection volume of 20% of the total blood processed. The substitution volume, administered pre- or post-dialyzer, depends on patient-specific factors [19]. Post-dilution HDF, the most prevalent method in Europe, achieves higher clearance levels for small and large molecules compared to pre-dilution, though Japan frequently uses pre-dilution [20]. Blood flow rates influence the convective volume achieved, with modern machines adjusting substitution volumes according to prescribed blood flow rates [21].

HDF offers a range of clinical benefits that improve cardiovascular health, reduce mortality, and enhance patient quality of life [22]. It optimally manages hyperphosphatemia, reduces inflammation, and improves anemia treatment through optimized erythropoietin response. Additional benefits include better hemodynamic stability, control over fluid overload, and reduced incidence of neurological symptoms, such as restless leg syndrome and polyneuropathy [23]. Importantly, HDF has shown efficacy in mitigating dialysis-related amyloidosis and joint pain [24]. Studies suggest that HDF, with its more extensive clearance capabilities, minimizes DNA damage and improves antioxidant status, with no observed adverse effects from potential depletion of beneficial molecules [17]. Observational studies show that HDF patients experience a reduction in all-cause and cardiovascular mortality by 14% and 33%, respectively [24,25]. Trials like the ESHOL study and the recent CONVINCE trial support these findings, with significant mortality reductions in the HDF group compared to HD. Notably, the CONVINCE trial highlighted a 23% reduction in all-cause mortality, particularly benefiting older patients, those with fistula access, and those without diabetes or cardiovascular disease.

HDF modalities include pre-dilution and post-dilution techniques, distinguished by the point of infusion relative to the dialyzer [26]. Pre-dilution HDF introduces replacement fluid before the dialyzer, requiring a larger convective volume to achieve comparable clearance to post-dilution [26]. Conversely, post-dilution HDF, the preferred method for adults and children, maximizes clearance efficiency, though at high ultrafiltration rates, it risks hemoconcentration and protein deposition in the dialyzer membrane [27]. A filtration fraction (FF) up to 30-35% of blood flow is recommended to prevent these complications. Advanced HDF machines automatically adjust the FF and replacement fluid rates to match blood flow changes, enhancing treatment safety and effectiveness [6].

Performing HDF requires specialized equipment and ultrapure water, underscoring the technical rigor of this method. Key machine features include precise ultrafiltration and fluid management systems to maintain hemodynamic stability, prevent hypovolemia or fluid overload, and ensure efficient solute removal [28]. Additional critical components include temperature control to prevent hypothermia and pressure monitoring to avoid filter clotting

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[29]. High-flux dialyzers designed for HDF must have an appropriate ultrafiltration coefficient (KUF) and other properties, while newer dialyzers, like medium-cutoff dialyzers, are avoided due to the risk of albumin loss. Ultrapure water is a non-negotiable standard for HDF, demanding sterile, pyrogen-free fluid infused directly into the patient's bloodstream [30]. Modern machines now produce this ultrapure fluid online, filtering it to remove bacteria and endotoxins, allowing for higher volumes essential for HDF.

The advances in HDF represent a substantial shift in renal replacement therapy, offering promising clinical outcomes and potential for becoming a conventional therapy alongside HD. The research supports the broader adoption of HDF, particularly with high convective volumes, and highlights the benefits in mortality reduction, quality of life, and treatment safety across patient demographics and global practices [31].

This study is important as it addresses the need for improved renal replacement therapies that enhance patient outcomes in chronic kidney disease management. HDF has shown promise in providing better control of biochemical parameters and improving cardiovascular health and overall well-being compared to conventional hemodialysis (HD). By specifically assessing HDF's impact on biochemical markers in Iraqi patients, this research adds valuable insights into HDF's effectiveness within a regional healthcare setting. The findings could help refine dialysis treatment protocols, potentially guiding broader clinical adoption of HDF in similar patient populations and improving the quality of care.

The aim of this study is to evaluate the effects and benefits of HDF on specific biochemical parameters in chronic hemodialysis (HD) patients over a six-month period following their transition to HDF. This retrospective study focuses on patients with end-stage renal failure treated in the HDF unit at Baghdad Teaching Hospital. By comparing biochemical measures such as urea, creatinine, electrolytes, hemoglobin, and calcium levels before and after six months of HDF therapy, the study aims to provide insights into HDF's impact on patient health and its potential advantages over conventional HD.

Methodology

Study design & Setting

A retrospective analysis was performed at the HDF unit of the Baghdad Teaching Hospital, Medical City Complex in Baghdad.

Study period

Duration of study was from the 1st of March 2024 to 1st of Octobers.

Study population

All patients diagnosed with end-stage renal disease (ESRD) and undergoing regular HDF were included in the present investigation. Both genders (male and female) were present throughout the research period and were chosen based on certain criteria.

Inclusion Criteria

The inclusion criteria for this study encompassed patients diagnosed with end-stage renal disease (ESRD) who had been receiving maintenance HDF therapy for a period exceeding three months but less than one year. Each patient followed a standardized HDF regimen, consisting of three sessions per week, with each session lasting four hours. Additionally, all enrolled patients were administered erythropoietin alfa (EPO alfa) at a dosage of 50–100 IU/kg twice weekly, along with a daily oral supplement of folate at 5 mg, ensuring uniformity in supportive treatment across the study cohort.

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Exclusion Criteria:

The exclusion criteria for this study were rigorously defined to ensure the selection of a stable patient cohort suitable for the assessment of HDF outcomes. Patients were excluded if they had been undergoing HDF for less than three months, had a diagnosis of acute kidney injury (AKI), or lacked arteriovenous fistula (AVF) as vascular access. Additional exclusion criteria included a history of immunosuppressive drug therapy, active inflammatory disease, clinical indicators of acute infection, liver disease, malignancy, or evidence of recent blood loss or gastrointestinal bleeding, all of which could confound the study results and impact the reliability of observed outcomes.

Sampling size

A convenient sample has been selected, which included 58 patients suffering from CKD who were attending a Baghdad teaching hospital in medical city for HDF.

Methods

- Initially, all patients were tested for hemoglobin and ferritin.
- All patients were then tested further for serum albumin, Urea, creatinine, Na, K, ca and PTH.

Sample collection and determination

The specimens of blood were obtained prior to the initiation of HDF. EDTA anticoagulant tubes were utilized for hematological specimens, but no anticoagulants were employed for other biochemical assays. The CBC was evaluated using the Celltac Es MEK-7300 automated hematological analyzer manufactured by Nihon Kohden, Japan. It encompassed hemoglobin (Hb), mean cell volume, mean cell concentration of hemoglobin, red cell distribution width (RDW), and serum ferritin.

Data collection

Data was obtained directly from records of patients at the dialysis facility.

Statistical Analysis

The data was converted into a computerized database format. Statistical analyses were conducted utilizing SPSS (Statistical Package for Social Sciences), Version 26 for Windows. Data are presented as mean ± standard deviation (SD), along with frequencies (counts) and proportions (%). It has been employed Student's t-test and one-way analysis of variance for mean comparisons. The Chi-square test was applied to evaluate frequencies and the significance of associations between categorical variables, with a P-value of ≤ 0.05 deemed statistically significant.

Results

The total sample of the study was 58 patients with mean age of 55.03±14.81 years. The most prevalent group was those over 45 years old, who constituted 65.5%. regarding to gender distribution the result showed more than third of the participants were male and 29.3% were female. As shown in Table 1 and Figure 1.

Table 1: distribution of study samples according to sociodemographic characteristic n=58

gender	Frequency	Percent
female	17	29.3

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male	41	70.7
Total	58	100
Age	Frequency	Percent
25-45 years	20	34.5
>45years	38	65.5
Total	58	100

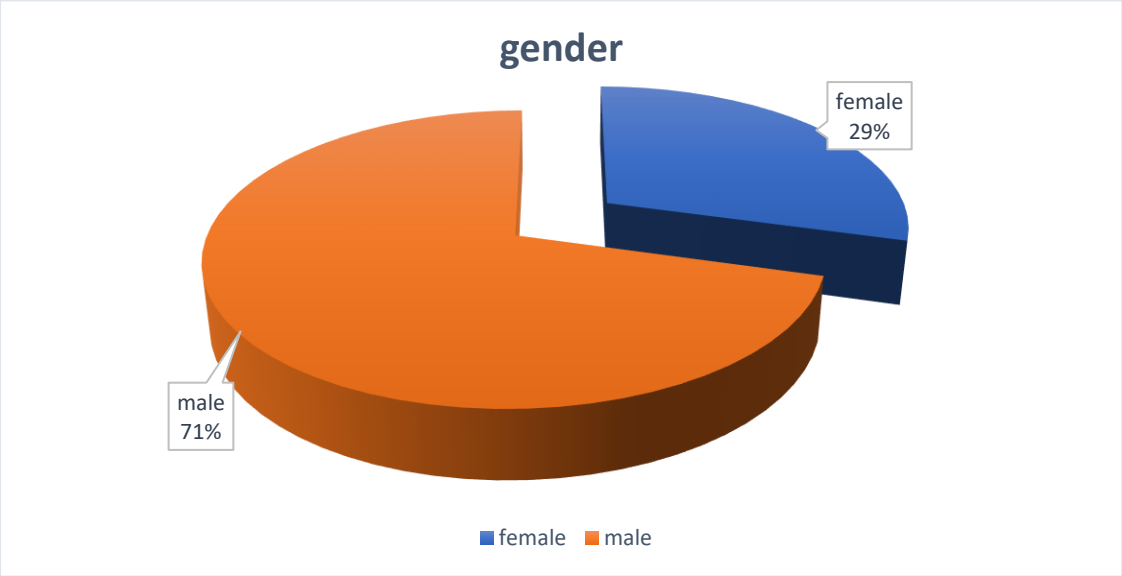

Figure 1: pie chart of distribution of study sample according to gender n=58.

In the present study, we compared the renal function test of participants at the time of the study and after 6 months from HDF therapy. Initially, the mean of blood urea was (60.03 mg/dL), and we found a decrease in the mean of blood urea after 6 months (46.09 mg/dL), with statically significant association (p=0.001) while (9.46 mg/dl) the mean of creatinine level at the baseline but after 6 months there was very slightly decrease to (9.17 mg/dL). Without any statistically significant correlation (p=0.344). As shown in Table 2 and figure 2.

Table 2: Comparison the mean of renal function test of participants during study time.

variables	no.	At baseline		After 6 months		P value
		Mean	S. D	Mean	S. D	
Urea (mg/dL)	58	60.03	20.789	46.09	15.775	**0.001***
Creatinine (mg/dL)	58	9.462	2.9139	9.178	2.5427	0.344
Paired sample test		df=57		statically significant*		

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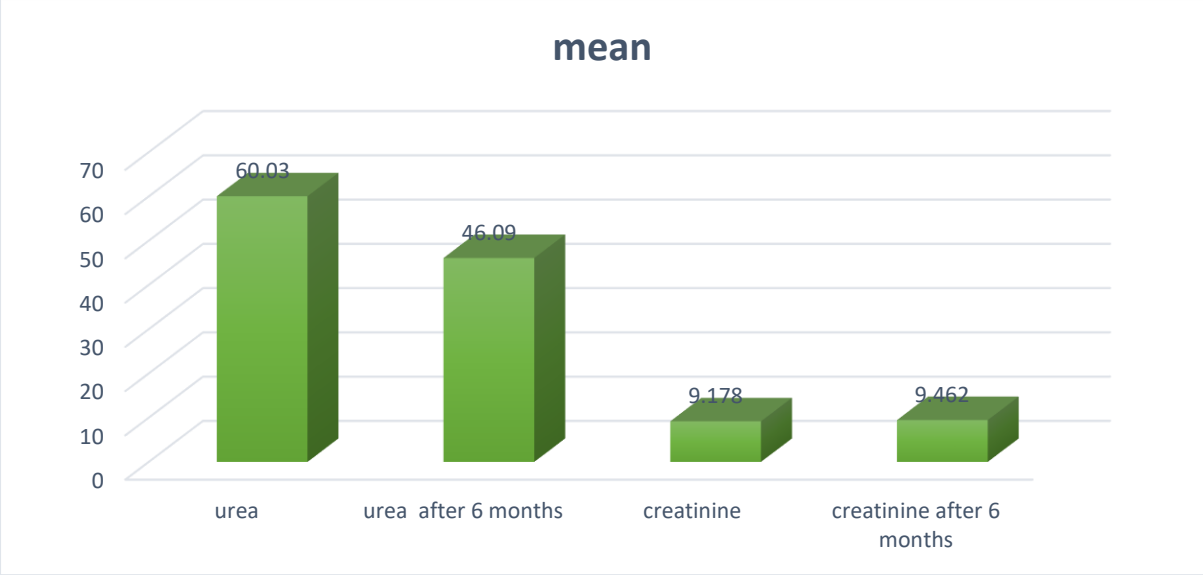

Figure 2: the mean of renal function test during study time.

Regarding the measurement of electrolyte among the study participants, the results showed at the beginning of the study that the mean of Na and K in the blood was (140.02 and 5.7 mm/l respectively), but after 6 months had passed, an decrease in the mean of Na was observed to (137.22 and 5.3 mm/l respectively), with statically significant association (p=0.001). There was a noticeable increase in the level of Ca in the blood after 6 months of the study periods to become (8.981 mg/dl), with significant correlation (P=0.001). As shown in Table 3

Table 3: comparison the mean of electrolyte test of participants during study time.

variables	no.	At baseline		After 6 months		P value
		Mean	S. D	Mean	S. D	
Na (mm/L)	58	140.02	4.411	137.22	4.713	**0.001***
K (mm/L)	58	5.709	1.1496	5.303	1.0365	**0.001***
Ca (mg/dl)	58	8.2017	1.23	8.981	1.40	**0.001***
Paired sample test		df=57		statically significant*		

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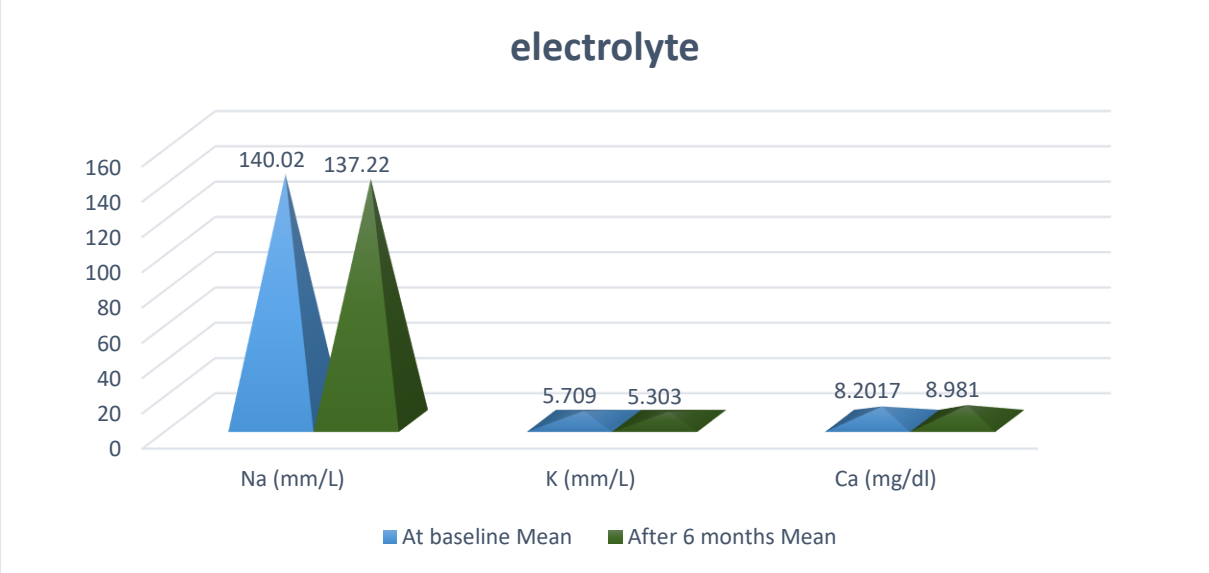

Figure 3: the mean of electrolyte test during study time.

In the current study of the measurement of hemoglobin and ferritin among the study participants, the results showed at the beginning of the study that the mean of Hb in the blood was (9.912 mg/dl), but after 6 months had passed, increase in the mean of Hb was observed to (10.42mg/dl). With statically significant association (p=0.029). There was a noticeable increase in the level of ferritin in the blood after 6 months of the study periods to become (682.98), but without any significant correlation (P=0.475). As shown in Table 4

Table 4: comparison the mean of hematocrit test of participants during study time.

variables	no.	At baseline		After 6 months		P value
		Mean	S. D	Mean	S. D	
Hb (mg/dl)	58	9.912	1.7855	10.426	1.6442	**0.029***
Ferritin (ng/ml)	58	643.81	375.64	682.98	389.375	**0.475**
Paired sample test			df=57	statically significant*		

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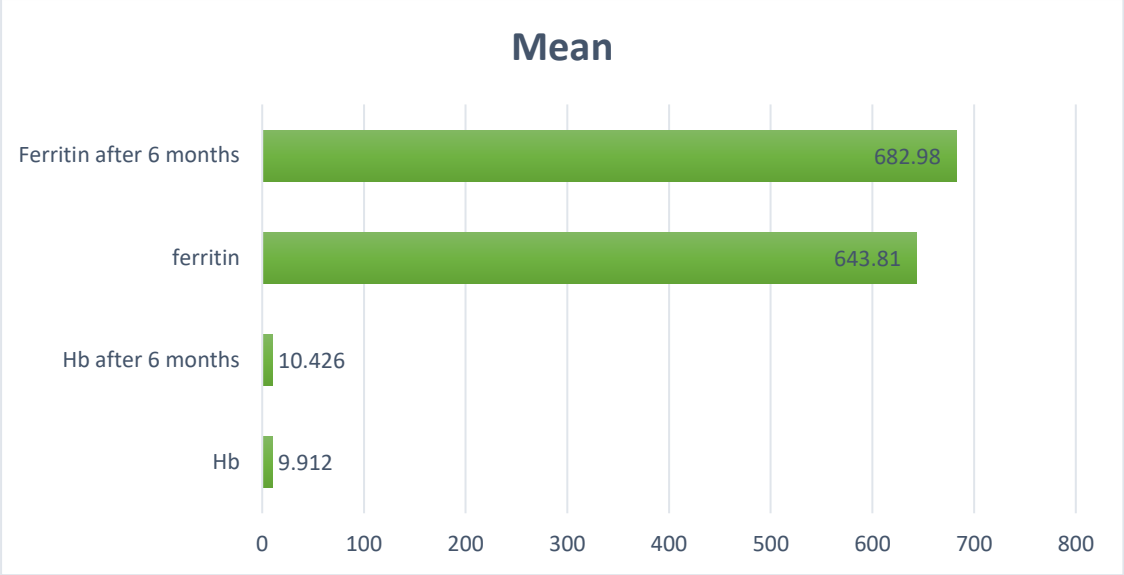

Figure 4: distribution of study samples according to hematocrit tests with time duration.

Comparing the PTH and albumin levels of participants at the time of the study. Initially, the mean of PTH and albumin levels was (286.31 mg/dL and 3.955 ng/ml respectively), and we found an increase in the mean of PTH and albumin levels after 6 months (299.36 mg/dL and 4.017ng/ml respectively), but without any statistically significant correlation (p=<0.05). As shown in Table 5.

Table 5: comparison the mean of PTH and albumin test of participants during study time.

variables	no.	At baseline		After 6 months		P value
		Mean	S. D	Mean	S. D	
PTH (mg/dl)	58	286.31	201.368	299.88	176.161	0.486
Albumin (ng/ml)	58	3.955	0.4964	4.017	0.4566	0.426
Paired sample test			df=57		statically significant*	

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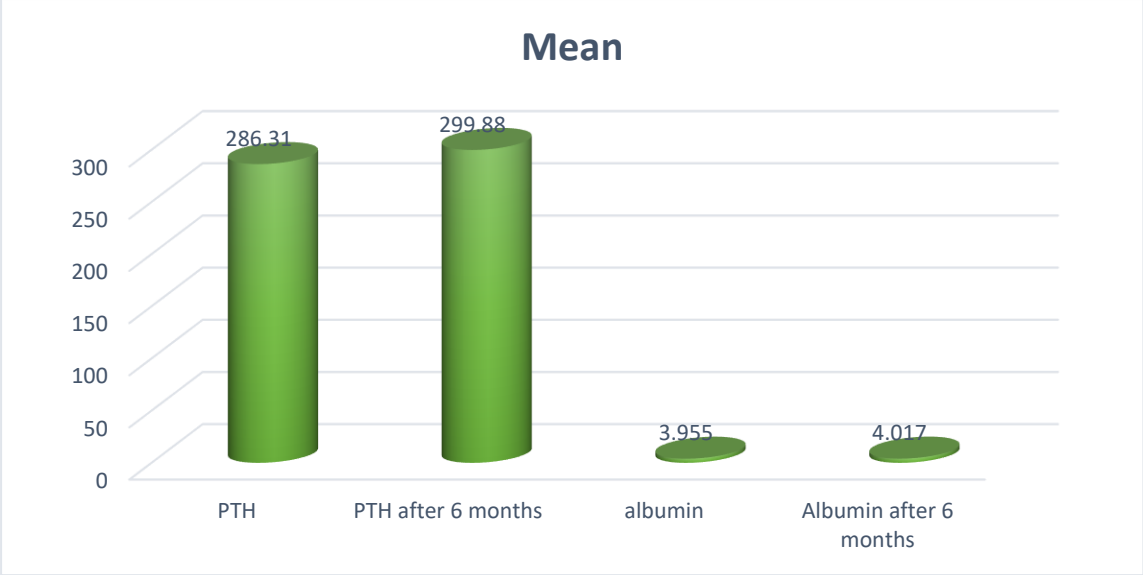

Figure 5: comparison the mean of PTH and albumin test of participants during study time.

Discussion

The kidney is crucial for regulating fluid, electrolyte, and acid-base balance; progressive renal function loss leads to dyselectrolytemia, which correlates with increased mortality in dialysis patients. The conventional formulation of the dialysate has undergone numerous disputes and modifications over time, aiming to restore electrolytic equilibrium via hemodialysis. The 'ideal' dialysate is a synthetic solution that encompasses all components of normal plasma, facilitating the removal of excess chemicals from the blood of uremic patients and the replenishment of certain elements in their bloodstream, through processes characteristic of hemodialysis [32].

HDF has emerged as the preferred substitute for kidney function in Europe and Asia owing to its superior efficacy compared to HD, specifically in the clearance and elimination of uremic toxins, enhanced intradialytic hemodynamic stability, diminished episodes of cardiac and vascular stress, and lowered inflammation [33,34]. This study sought to evaluate the extent to which HDF treatment impacts several parameters.

In the current investigation, patients with chronic kidney disease exhibited baseline serum urea levels that were substantially beyond the normal range. After six months, there was a significant decrease in serum urea levels, with most patients' levels dropping to 46 mg/dl. The serum creatinine concentration was significantly over the normal range (9.1 mg/dl) in chronic kidney disease patients undergoing HDF at baseline, with a little increase after six months (9.46 mg/dl). This aligns with the research performed by Mohammad DK , which indicated that serum creatinine and urea levels were dramatically reduced. Urinary excretion and dialysis are pivotal in retaining metabolites such as water, electrolytes, urea, and creatinine. The augmented production of metabolites via catabolic procedures and alternatives metabolic pathways also exerts an effect. This obstruction to excretion, coupled with a persistent elimination of creatinine from muscle, results in an accumulation of creatinine in total body water, consequently leading to an elevation [35]. This outcome aligns with the research carried out by Pedrini LA, et al. [36]. A different investigation demonstrated a more rapid decline in renal function tests, specifically urea clearance or creatinine levels. The impact became visible four

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months post-randomization and persisted after twelve months [37]. The research conducted by Ning et al. [38] showed serum creatinine levels at 24 and 48 hours, revealing a significant reduction at both time points; however, no significant drop was observed at 72 hours. Cui et al. [39] did not observe alterations in levels of creatinine in the serum within the research sample. The discrepancy may be attributed to differences in the size of specimens and target populations.

The testing of electrolytes among the research participants revealed a drop in the mean levels of Na and K, with a statistically significant correlation (p=0.001). A considerable increase in blood calcium levels was seen after six months of the research period, with a notable correlation (P=0.001). This conclusion is analogous to the findings of investigations done by Baeg SI et al. [40] and Maduell F et al. [41]. The subsequent segment of the trial aimed to assess biochemical and clinical outcomes. Following a six-month course of online HDF, the treatment was administered for a duration of six months. Plasma tests including intact parathyroid hormone, phosphorus, calcium, bicarbonate, uric acid, potassium, salt, creatinine, and urea were performed weekly each month. Intact Parathyroid Hormone (iPTH). A considerable reduction in the levels of urea, creatinine, and uric acid was observed throughout a 6-month period. The biochemical data indicate that parathyroid hormone, bicarbonate, potassium, and sodium levels drop after 6 months of HDF treatment, although phosphorus and calcium levels are lower than baseline. Serum calcium levels were diminished prior to dialysis, likely attributable to the kidneys' role in converting vitamin D to its active metabolite, essential for intestinal calcium absorption. In patients with renal failure, the kidneys are largely compromised, resulting in decreased vitamin D levels. Elevated serum calcium greatly enhanced erythropoietin production. Marrero et al. [42] revealed that EPO binding to its receptor activates a cytosolic tyrosine kinase, which then catalyzes the tyrosine phosphorylation and activation of phospholipase C. The hydrolysis of phosphatidylinositol 4, 5-bisphosphate by the latter cause results in the production of inositol 1, 4, 5-triphosphate. These processes result in a biphasic increase in Ca+2, characterized by an initial release of Ca+2 from intracellular reserves, succeeded by the influx of Ca+2 by erythropoietin receptor-operated, voltage-independent channels. The alteration in serum sodium results from a reduction in renin secretion from the kidney, which is crucial for sodium regulation, due to significant renal dysfunction [43].

Regarding the measurement of hematocrit in the current study, the results showed a significant increase in the average hemoglobin level after 6 months of HDF treatment, as well as a very slight increase in the serum ferritin level. This result is consistent with the study conducted by Buoncristiani et al. [44], which showed an increase in hemoglobin levels after 6 months of repeated HDF therapy. Also, in the study by Kooistra *et al.* [45] and the study by Lee YH et al. [46] of the 179 only 44 converted to HDF and were maintained for more than 12 months. Found the Hgb level increased significantly in patients after they were converted to HDF. Although several studies have reported no changes in anemia control in patients undergoing HDF [47–49]. The possible explanation for this difference may be due to variations in sample size, sitting of study and target populations.

The concentration of hemoglobin, red blood cells, has significantly increased after the dialysis procedure. Therefore, as expected, the deficiency in erythropoietin production significantly contributed to the onset of anemia. Moreover, chronic renal failure (CRF) groups showed a significant decrease in hemoglobin and hematocrit levels. It was observed that treating patients with dialysis successfully reverses anemia in patients suffering from uremia. Moreover, the

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increases in hematocrit and hemoglobin were partially explained by an increase in the number of red blood cells. Furthermore, angiotensin II can indirectly enhance the formation of red blood cells through its stimulatory effect on the adrenal cortex cells to secrete androgens [50]. Adamson [51] predicted that erythropoiesis involves the close interaction between iron and erythropoietin. At its core, erythropoietin is the catalyst that drives the formation of red blood cells. Iron is the main source to produce new red blood cells.

Another study by Mohamed EA et al. [23] found significant increase in hemoglobin and ferritin after 12 months from HDF. Furthermore, Georgatzakou et al., [52] described that mean Hb was non-significantly increased after therapy in HD group, however it was significantly increased in HDF group after treatment. As well, Mohamed et al., [53] revealed that HDF have significantly higher positive impact on anemia parameters when compared to HD treatment. However, Smith et al., [54] described that there was no significant variation in anemia parameters, the same results were reported by in adults and Galal & Hesham, [55]. This disagreement with our results may be due to the differences in sample size and inclusion criteria as well as the differences in study settings.

Comparing the PTH and albumin levels of participants at the time of the study. we found an increase in the mean of PTH and albumin levels after 6 months this results similar to study by Mohamed EA et al. [25] that showed increase the albumin and PTH after 12months but No statistically significant variation was found among groups. Similarly, current study Ibrahem et al., [56] reported that the HDF group was related to significantly greater levels of albumin & intact PTH. Also, Smith et al., [54] reported that Serum albumin levels statically increase. However, Galal & Hesham [55] revealed that showed no significant difference in albumin levels in HDF studied cases compared to HD patients. While the Pedrini et al., [57] revealed that there were no clear variations in clinical parameters' albumin and parathyroid hormone were observed HDF groups over time.

Conclusion

There was a significant impact and benefit of HDF on patients with chronic kidney failure after 6 months, with a substantial increase in certain biochemical parameters (hemoglobin and calcium) while other parameters significantly decreased (Na, K and urea).

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