

Study of Related Biochemical Tests and PTH in End Stage Renal Disease Patients in Iran

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Abstract

Introduction: End-stage renal disease (ESRD) patients usually have abnormalities in various laboratory tests. The aim of this study is evaluating of the rate of various laboratory tests in ESRD patient to reduce the risk of mortality and prevent them of other diseases.

Methods: In this cross-sectional study a total of 300 patients who had ESRD and had been on hemodialysis treatment for at least 6 months were selected. The laboratory tests consisted of measurement of high density lipoprotein, triglyceride, cholesterol, fasting blood sugar, parathyroid hormone, alanine transferase, aspartate transferase, alkaline phosphatase, creatinine, blood urea nitrogen, calcium, phosphorous, sodium, potassium, and albumin.

Results: The study population included 52.3% males and 47.7% females with average age of 41.5 ± 14.3 years. The high serum level of Chol (>200 mg/dL) and TG (>160 mg/dL) are 48.7%, 32.3%, respectively. About 98% were in high risk of range HDL (<45 mg/dL). All of participants had over normal range of BUN and about 96% of them were over normal range of Cr. Rate of high serum level of Na, K, P, and Ca were 3.7%, 52%, 54.3%, and 14.6%, respectively.

Discussion: Depend the result of this study, can understand that great group of patients with ESRD have high risk serum level of lipid indexes. Recent studies showed that there is a clear correlation between HDL cholesterol and cardiovascular risk in ESRD patients and there is correlation between level of triglyceride level and CKD progression. The important risk factors for involving in ESRD are hyperphosphatemia, hypercalcemia, dyslipidemia, and hypoalbuminemia which impact on CVD morbidity directly.

Conclusion: In this study observed that most of patient with ESRD have abnormality in their lipid profiles factors, mineral electrolytes factors, and PTH. Regular laboratory checkup can control renal failure (especially ESRD patients) patients. Proper care of body, balanced diet intake, plenty water intake during the day can help them to control these diseases.

Keywords: Biochemical tests; ESRD; PTH

Introduction

According to previous studies, reason of fifty percent of mortality in end stage renal disease (ESRD) is cardiovascular [1]. End stage renal disease may itself be in part ischemic, related to large atheroma, arteriosclerosis disease. Blood pressure is a cause of advancing renal failure; while, ESRD can increase arterial disease and cardiac failure [2]. ESRD patients often suffer from various cardiovascular diseases (CVD), which account for considerable morbidity and mortality. In addition, diabetes mellitus (DM), which comprises the most common cause of ESRD, is a major risk factor for CVD [3]. Infectious diseases are the second-most common cause of death (after cardiovascular disease) in ESRD patients. Cardiovascular diseases and infections account for 50% and 20% of deaths in ESRD patients, respectively [4]. ESRD patients usually have increased concentrations of triglyceride-rich lipoproteins and reduced serum levels of high density lipoprotein (HDL) cholesterol [5]. However, low-density-lipoprotein (LDL) cholesterol values were found to be within normal limits or reduced in this population. The common lipid abnormalities in CKD patients include low HDL, hypertriglyceridemia while LDL and total cholesterol may be low, normal or high. Dyslipidemia has a vital role in occurrence of CVD in patients with chronic kidney disease [6]. In other hand, 50% of renal patients were involving in dyslipidemia [7]. Another study showed that renal dysfunction was associated with both reduction in serum HDL concentration and increased circulating monocyte count [8]. While CKD is a global public problem, patients with CKD have higher risk of progression to ESRD. The out range of lipid indexes are associated with declining of glomerular filtration rate (GFR)

[9]. Most patients with CKD have mixed dyslipidemia and the lipid profiles are highly atherogenic with adverse changes in all lipoproteins [10]. Epidemiological data indicated that approximately 10% of adult population have some form of chronic renal disease that eventually may progress into a complete loss of kidney function [11]. In addition, CVD mortality is significantly higher in HD patients than general population [12]. An important way of diagnose and treat CVD patients is checking dyslipidemia; which is a great risk factor for involving in CVD [7]. This affect is characterized by a progressive loss of renal function; in end-stage kidney disease, the patient requires dialysis or kidney transplantation to survive [13].

Studies showed that several factors such as hyperlipidemia, hyperglycemia, and hyperuricemia are risk factors for involving in ESRD [14].

The increases amount of mineral electrolytes like potassium (K),

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phosphorous (P), calcium (Ca), and sodium (Na) and also parathyroid hormone (PTH) have impact on reduction of kidney function [15].

As we know, there is limited information on the medical laboratory tests in ESRD Patients in Iranian populations. Therefore, the association of various tests and ESRD needs to be further evaluated in Iranian populations. The aim of the present study was to evaluate lipid indexes, mineral electrolytes, PTH, and related biochemical tests in ESRD patients, eventually to reduce the risk of mortality and prevent them from other diseases.

Methods and Materials

In this cross-sectional study a total of 300 patients who had ESRD and had been on regular dialysis treatment for at least 6 months were enrolled.

Exclusion criteria were age >70 years and unwillingness to participate in this study. Also clinically unstable patients and those with tumors, diabetes mellitus, inflammatory diseases (such as diabetic ulcers of chronic pulmonary disease, systemic lupus erythematosus, rheumatoid arthritis, and tuberculosis infection) or those treated with immunosuppressive drugs were excluded. No patients showed signs of inflammation or infection during the study period.

Body temperature was measured before each dialysis session and was never elevated. Informed written consent was obtained from all enrolled patients prior to the study. The required information regarding each patient was gathered through predesigned questionnaires including the patient's medical history, clinical examinations and laboratory findings. All ESRD patients were treated three times weekly with standard bicarbonate dialysis with semi-synthetic dialysis membranes. The laboratory tests consisted of measurement of high density lipoprotein, triglyceride, cholesterol, fasting blood sugar,

parathyroid hormone, alanine transferase, aspartate transferase, alkaline phosphatase, creatinine, blood urea nitrogen, calcium, phosphorous, sodium, potassium, and albumin using high sensitive ELISA kits. The creatinine was measured using Zist Chimi kits (Tehran, Iran).

Statistical package for social sciences (SPSS v.21, IBM Inc., Chicago, IL, USA) software was used for analyzing the data. Quantitative variables were described as mean and standard deviation while qualitative variables were described as frequency and percent.

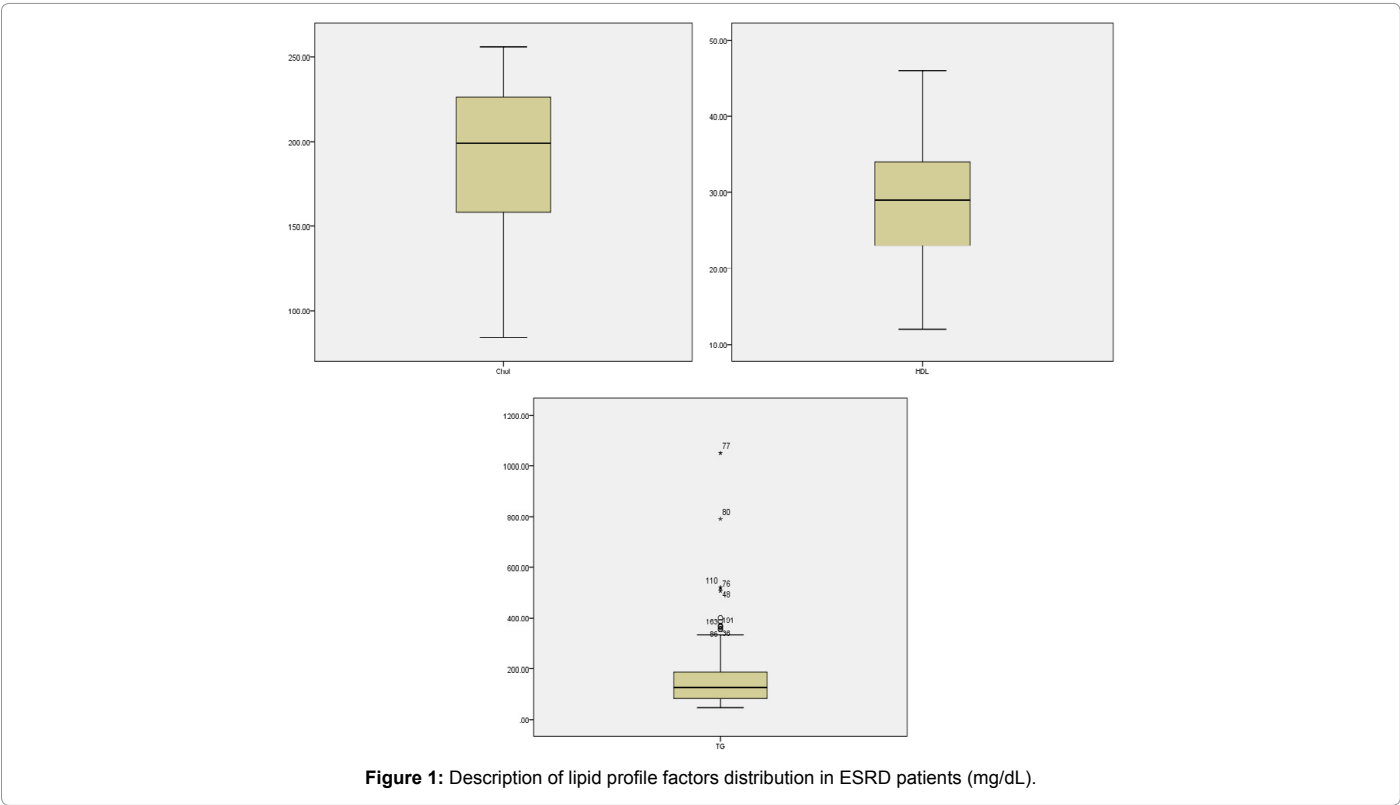
Results

Three hundred ESRD patients participate in this study. The study patients included 157 males (52.3%) and 143 females (47.7%) with average age of 41.5 ± 14.3 years. The mean Creatinine (Cr) and Blood urea nitrogen (BUN) were 8.65 ± 5.8 and 50.67 ± 12.2 , respectively.

The mean Chol, TG, and HDL are 190.47 ± 42.5 mg/dL, 156.79 ± 108.9 mg/dL, 29.12 ± 7.6 mg/dL. The high serum level of Chol (>200 mg/dL) and TG (>160 mg/dL) are 48.7% (146), 32.3% (97), respectively. The percentage of population of high risk range of HDL was 98.3% (297) (<45 mg/dL). There is no correlation between subjects' chol and TG ($r=-0.079$, $p=0.173$) (Table 1 and Figure 1).

Test	Range	Value
High density lipoprotein (HDL)	≤45 mg/dL	297 (99%)
	>45 mg/dL	3 (1%)
Triglyceride (TG)	≤160 mg/dL	203 (67.7%)
	>160 mg/dL	97 (32.3%)
Cholesterol(chol)	≤200 mg/dL	154 (51.3%)
	>200 mg/dL	146 (48.7%)

Table 1: Description of lipid profile of ESRD patients.



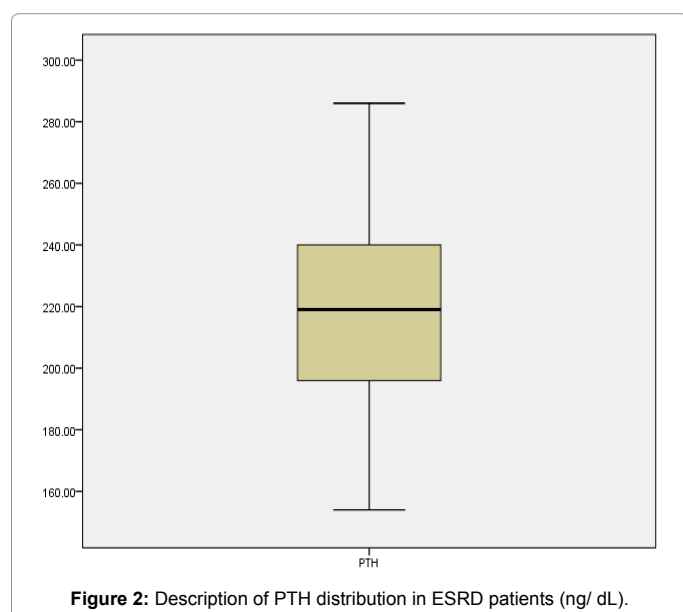
The mean Alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) were 19.05 ± 3.9 , 22.85 ± 4.6 , and 445 ± 594.6 , respectively.

All of participants had over normal range of BUN (>20 mg/dL) and about 96% of them were over normal range of Cr (>1.6 mg/dL). All participants were observed in normal range of ALT and AST. Other important tests were indicated in Table 2. An considerable result was PTH that all participants' were over normal range (Figure 2).

The mean Na, K, Ca, and P were 139.19 ± 3.2 , 5.11 ± 0.5 , 9.3 ± 0.8 , and 5.04 ± 1.5 , respectively. Rate of high serum level of Na, K, P, and Ca were 3.7%, 52%, 54.3%, and 14.6%, respectively (Table 3, Figures 3 and 4).

Test	Range	Value
Blood urea nitrogen (BUN)	<7 mg/dL	-
	7-20 mg/dL	-
	>20 mg/dL	300 (100%)
Creatinine (Cr)	<0.6 mg/dL	-
	0.6-1.2 mg/dL	-
	>1.2 mg/dL	300 (100%)
Alkaline Phosphatase (ALP)	<44 IU/dL	-
	44-147 IU/dL	10 (3.3%)
	>147 IU/dL	290 (96.7%)
Alanine transaminase (ALT)	7 units/L	-
	7-56 Units/L	300 (100%)
	56 units/ L	-
Aspartate transaminase (AST)	<10 Units/L	-
	10-40 Units/L	300 (100%)
	>40 Units/L	-
Parathyroid hormone (PTH)	<10 ng/ dL	-
	10-65 ng/ dL	-
	>65 ng/ dL	300 (100%)
Albumin (ALB)	<3.5 g/dL	-
	3.5-5.5 g/dL	300 (100%)
	>5.5 g/dL	-
Fasting blood sugar	≤ 110 mg/dL	210 (70%)
	>110 mg/dL	90 (30%)

Table 2: Description of various laboratory test among ESRD patients.



There was a correlation between BUN and P ($r=0.277$, P value <0.001). There were not any correlation among lipid profile factors and mineral electrolytes.

Discussion

This study, evaluate 300 patients who had ESRD and had been on regular dialysis treatment. Various laboratory tests were performed to evaluate the renal function in ESRD patients. Various laboratory tests included Lipid profile factors, mineral electrolytes, PTH, and related biochemical tests. At first, because they were in end stage of renal disease, all of participants had high serum level of BUN and 96% of them had high serum level of creatinine.

Depend the results of this study, can understand that great group of patients with ESRD were in high risk serum level of lipid indexes. In other hand, dyslipidemia like high level of triglycerides as an important risk factor for atherosclerosis in HD patients was associated with chronic kidney disease [16]. Furthermore, our study showed that about 99% of participants were in risk range of HDL which increase the rate of cholesterol sedimentation in various organs especially cardiovascular system. Also, a significant number of them had high serum level of TG and Chol (32.3 5 and 48.7%, respectively) which can confirm the past studies reports. There are many mortality and occurrence of CVD among ESRD patients; while, mortality among HD patients is above 20% per year that fifty percent of them is related to CVD [17]. Another study showed that there is a significant correlation between HDL cholesterol and cardiovascular risk in ESRD patients [18]. Reduction the levels of serum apolipoprotein A-I (apoA-I), apolipoprotein A-II (apoA-II), HDL cholesterol and HDL phospholipids, and elevated levels of HDL-triglycerides are HDL abnormalities that could be seen in patients on dialysis [19].

A study in USA expressed that there is direct correlation between level of triglyceride level and CKD progression [20]. In addition, high level of TG was associated with rising in serum creatinine [21]. Also, this correlation was observed in our study (P value=0.01). A cohort study indicated that 20% of hypertriglycemia patients had high serum level of creatinine [21].

Fibroblast growth factor 23 increases in renal failure to prevent the hyperphosphatemia. Assessing this factor in primary stage of renal diseases help to prevent from ESRD [22]. Actually, it was assessing by other researcher but we will do it in our next study to evaluate it in Iran.

Several studies have shown an association between increased risk of mortality and greater PTH and calcium levels in ESRD patients. Previously published studies have been performed on North American, Japanese and European populations and there were no data available from the Iranian ESRD patients [23]. Depend on studies the important risk factors for involving in ESRD are hyperphosphatemia, hypercalcemia, dyslipidemia, and hypoalbuminemia which impact on CVD morbidity directly. Especially, over normal range of P is a great risk factor of CKD patients [24,25]. Recent study indicated that 52.9% and 52% had hyperphosphatemia and hyperkalemia, respectively. These results were in accordance with several studies from a large population which has shown high serum phosphorus, PTH, and calcium levels in ESRD patients.

All of our study population were in normal range of albumin; while, hypoalbuminemia observed in ESRD patients of other studies [24].

A systematic review-Meta analysis study which analyzed cohort studies of mineral electrolytes and PTH in CKD, expressed that

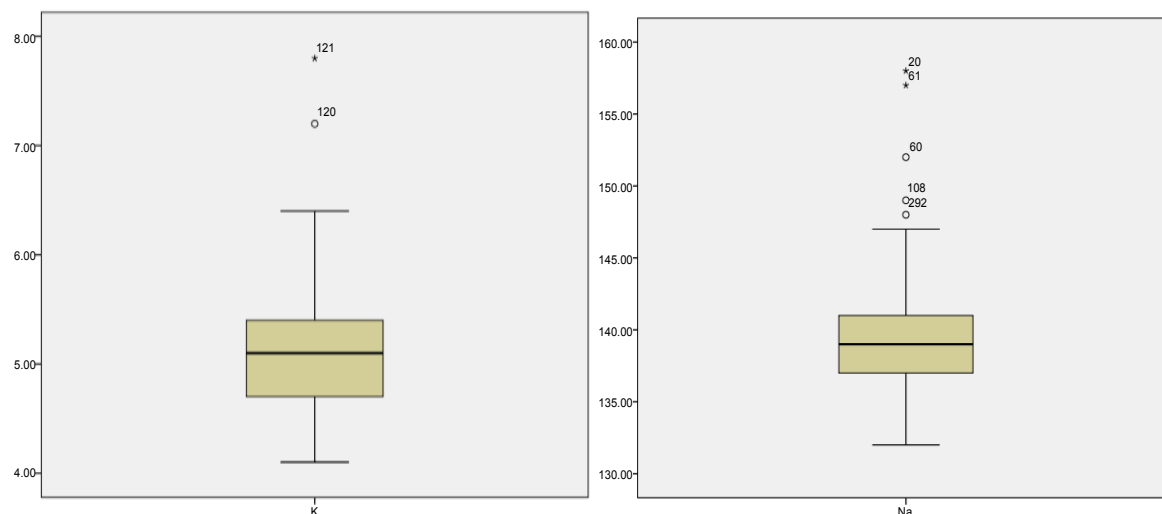


Figure 3: Description of sodium and potassium distribution in ESRD patients (mEq/L).

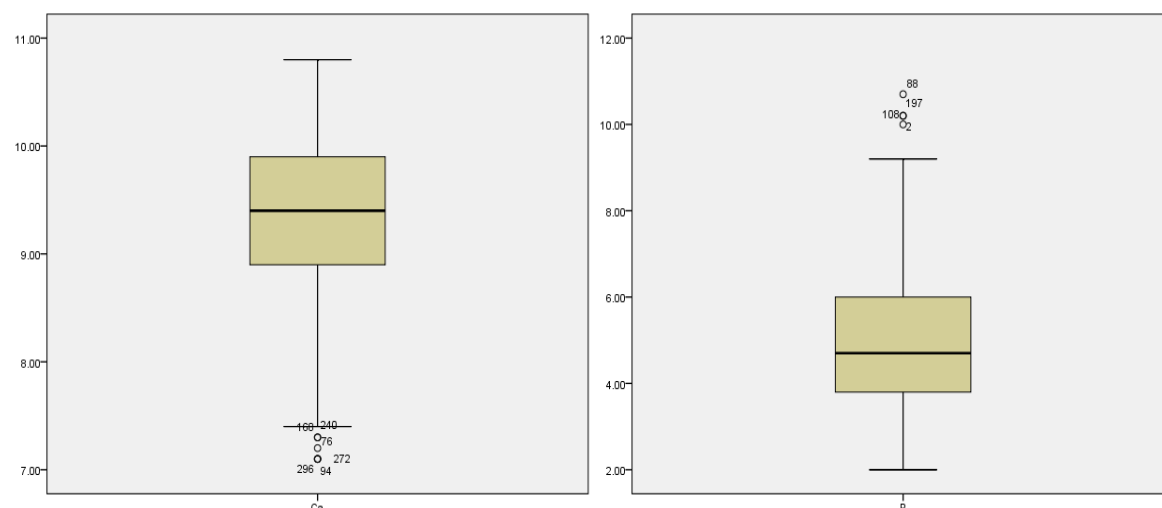


Figure 4: Description of calcium and phosphorous distribution in ESRD patients (mg/dL).

Test	Range	Value
Sodium (Na)	<135 mEq/L	13 (4%)
	135-145 mEq/L	277 (92.3%)
	>145 mEq/L	11 (3.6%)
Potassium (K)	<3.5 mEq/L	-
	3.5-5 mEq/L	145 (48%)
	>5 mEq/L	157 (52%)
Phosphorous (P)	<2.5 mg/dL	3 (1%)
	2.5-4.5 mg/dL	135 (44.7%)
	>4.5 mg/dL	164 (52.9%)
Calcium (Ca)	<8.5 mg/dL	42 (13.9%)
	8.5-10.2 mg/dL	216 (71.5%)
	>10.2 mg/dL	44 (14.6%)

Table 3: Description of electrolyte factor among ESRD patients.

can't approve the correlation of mortality and morbidity with rate of serum calcium and parathyroid hormone, but can confirm that there is a significant correlation between rates of serum phosphorous with mortality. In comparison, this systematic review study expressed that a

cohort study mentioned that there is a correlation between P, Ca, and PTH of serum with mortality among CKD patients [26].

A cooperative study carried out by Noordzij et al. in the Netherlands, reported that the attendance of plasma phosphorus concentrations greater than the KDOQI targets increased mortality risk in hemodialysis and peritoneal dialysis patients [27].

Another important factor which increased among CKD patients is PTH. In addition, an important complication of high PTH level is cardiovascular disease [28]. As renal function continues to decline, the activation of vitamin D by the kidney is decreased and low levels of activated Vit D fail to suppress PTH, so hyperparathyroidism occurs in CKD patients [29]. Present study indicated that all participants have over normal range of PTH; while, its mean was 219.2 ± 25.8 . Studies showed that over normal range of PTH is associated to mortality increasing. An important treatment in CKD patients is keeping PTH in normal range [28]. In addition, 14.6% of our participants had hypercalcemia which can be related to hyperparathyroidism hormone.

Also, Ca, P and vit D have a great deal with mortality among HD patients, in other hand, better survival of HD patients are associated with suitable range of P, vit D, and Ca [28,30]. However, mortality among hypophosphatemia patients didn't observe [31].

Studies showed that diabetes mellitus is a significant risk factor for involving in ESRD [32]; However, patients with diabetes mellitus were excluded of our study but 30% of our participants were in high serum level of FBS (>110 mg/dL).

An experimental study was performed in 16173 hemodialysis patients, showed that elevated calcium, phosphorus and PTH levels were associated with increments in all-cause mortality [33]. Furthermore, the study was examined in 13792 patients treated in European medical care facilities, showed that patients with PTH, calcium and phosphate levels within the KDOQI target ranges have the lowest risk of mortality compared to those outside the target ranges [34].

In addition, chronic renal disease and hemodialysis patients are more exposed to chronic liver disease especially viral hepatitis like hepatitis B [35]. This study assessed the rate of ALT and AST among participant. At first to indicate there were no abnormalities in this factors and they don't have any hepatitis. So all of ESRD patients were in normal range.

In addition, increasing the amount of ALP was seen in dialysis patients and was associated with increased mortality. ALP is an essential part of serum calcification [36]. Collagen calcification can be prevented by inactivation of ALP [37]. Clinical studies have demonstrated that high serum ALP to be related to coronary artery calcification in patients with hemodialysis [38]. The study was conducted by Abramowitz et al. reported that $ALP > 10^4$ u/l was related to 65% higher risk of death in patients with $eGFR \geq 60$ ml/min/1.73 m² [39]. Based on the results from the dialysis outcomes and practice patterns study (DOPPS) demonstrated that 25% elevated risk of death and 30% elevated the risk of hospitalization in patients with mild to severe increased ALP compared to normal controls [40].

Thus, assessment of lipid profile factors, mineral electrolytes, PTH, and related biochemical tests may be useful for the treatment monitoring in clinical practice in patients with ESRD.

According to this study can be understood that by regular laboratory checkup can control ESRD patients. In other hand, most of patient with ESRD have abnormalities in their lipid profiles parameters, mineral electrolyte parameters, and parathyroid hormone. Proper care of body, balanced diet intake, plenty water intake during the day, and check up their medical laboratory test can help them to control and prevent them from these diseases.

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Conflict of Interest

There is no conflict of interest.

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