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Study of some physiological parameters in patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD)

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Abstract

Autosomal dominant polycystic kidney disease (ADPKD) is the most common Mendelian disorder of the kidney and affects all racial groups worldwide. It is characterized by focal development of renal and extrarenal cysts in an age-dependent manner. This study tested some physiological parameters in two groups of patients with ADPKD, the first group included patients with kidney failure and the second group included patients without renal failure as well as the control group. The study showed an increase in urea and uric acid in the serum of the patients without renal failure compared with the control levels and were higher in the patients with renal failure compared with the patients without renal failure, which amounted to 115.8 mg / dL and 10,278 mg / dL and 22.45 mg / dL and 7,264 mg / dL and 11.03 mg / dL and 3,264 mg /dL respectively. Creatinine serum level was higher in the patients with renal failure compared with the patients without renal failure and control, reaching 3.5 mg / dL , compared with 1,026 mg / dL and 0986 mg / dL , respectively. Potassium ion level was higher in patients without renal failure than in control reaching 4,179 mmol / L and 2.34 mmol / L, respectively, while the level was higher in patients with renal failure than in patients without renal failure where it reached 7.09 mmol / l. Sodium ion levels were low in the patients with renal failure and the patients without renal failure than in the control group, reaching 87.06 mmol / l and 129 843 mmol / l and 147.25 mmol / L, respectively. The level of sodium ion was lower in the patients with renal failure than in the patients without renal failure. Results of the study showed normal levels in serum albumin and liver enzymes, AST and ALT.

Key words: Autosomal Dominant Polycystic Kidney Disease, physiological parameters.

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a systemic hereditary disorder that affects more than 12.5 million individuals worldwide. Thus, ADPKD is the most common life-threatening hereditary genetic disease, compared to the numbers of individuals affected by cystic fibrosis, Down's syndrome, hemophilia, muscular dystrophy, and sickle cell anemia, combined [1]. ADPKD is inherited as an autosomal dominant trait with complete penetrance. ADPKD is characterized by progressive formation and enlargement of renal filled-fluid cysts resulting in abnormal kidney structure and renal insufficiency. End-stage renal disease (ESRD) will be observed in 50% of cases by the fifth decade [2]. Numerous renal and extra-renal manifestations have been described for ADPKD. Hypertension, left ventricular hypertrophy, cardiac valvular defects, back and abdominal pain, cerebral aneurysms, and liver cysts are the most important clinical findings. Overall, it accounts for approximately 5% of ESRD in developed countries [3,4].

It is genetically heterogeneous with two genes identified, PKD1and PKD2. PKD1 gene locates to chromosome 16 and responsible of 85% of ADPKD cases, while PKD2 gene locates to chromosome 4 that responsible of the remained cases. Although the phenotypes of PKD1 and PKD2 overlap completely, PKD1 is associated with more severe renal disease with an earlier clinical presentation

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and an excess of premature mortality [3,5]. Polycystins 1 and 2, the gene products of PKD1 and PKD2, are transmembrane proteins that are components of a novel multifunctional signaling pathway. Polycystin 1 may function as a receptor involved in cell– cell and/or cell–matrix interaction. By contrast, polycystin 2 functions as a subunit of a cation channel with nonselective permeability. Both proteins interact through their cytoplasmic region and transmit fluid flow–mediated mechanosensation, which is detected by the primary cilium of renal epithelium. Disruption of normal polycystin function by mutations predispose to cyst formation through loss of mechanical cues in tubular epithelial cells that regulate tissue morphogenesis [6,7]. In view of the scarcity of studies on ADPKD in Iraq came this study to shed light on some aspects of physiological criteria which relates to this disease.

Materials and Methods

The study included twenty-four affected persons with ADPKD (15 men and 9 women) who were receiving treatment at Al-Hakeem General Hospital and Al-Sadr Medical city in the province of Najaf. Diagnosis of affected persons was confirmed by ultrasound imaging to detect the presence of renal cysts and according to Ravine criteria [8]. The patients were divided into two groups, one included ten ADPKD patients with renal failure and the other comprising fourteen ADPKD patients without renal failure. Fifteen healthy persons, were had age mean nearly equal to the age means of the patients, considered as control group. Blood samples were taken at 5 ml from each person. The study included the following:

1. Kidney function criteria:
   - Serum urea was estimated according to BioMerieux Kit (France).
   - Serum uric acid was determined according to Spinreact Company Kit (Spain).
   - Serum creatinine was estimated according to Biolabo SA Kit (France).
   - Serum albumin was assessed according to procedure of Spinreact Company Kit (Spain).
2. Electrolytes: K^+ and
   - A potassium ion (K+) level in serum was estimated According to Spinreact company kit (Spain).
   - A sodium ion (Na+) level in serum was assessed according to Spinreact company kit (Spain).
3. Liver function tests: Aspartate transaminase (AST) and alanine transaminase (ALT) enzymes were assessed in the serum according to Spinreact company kits (Spain).

Statistical analysis of the results was performed by using megastat program (version 10.12) for excel 2007; t-test and one way ANOVA test were used to comparison between the groups.

Results

1. Kidney function criteria:

Table (1) indicated a significant increase ($P \leq 0.05$) in serum urea concentration in the ADPKD patients (61.346 ± 9.811) mg/dL in comparing with control group (11.03 ± 0.629) mg/dL, also a significant increase serum creatinine and uric acid concentrations (2.057 ± 0.261) mg/dL and (8.52 ± 0.381) mg/dL in comparing with control group (0.968 ± 0.047) mg/dL and (3.984 ± 0.275) mg/dL respectively. The results revealed non-significant differences in albumin concentrations between the ADPKD patients (4.089 ± 1.4) mg/dL and control group (3.78 ± 0.134) mg/dL.

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Table (1): Kidney criteria in the ADPKD patients and control group.

Groups / Kidney Criteria	Mean ±S.E.	
	Control N=10	**Patients N=24**
Urea: mg/dL	11.03 ± 0.629	61.346 ± 9.811 *
Uric acid: mg/dL	3.984 ± 0.275	8.520 ± 0.381 *
Creatinine: mg/dL	0.968 ± 0.047	2.057 ± 0.2619 *
Albumin: g/dL	3.786 ± 0.134	3.297 ± 0.691

(*): significant difference (P≤0.05).

Figure (1) showed a significant increase (P≤ 0.05) in serum urea concentration in the patients with renal failure (115.8 ± 3.214) mg/dL than the patients without renal failure (22.45 ± 2.24) mg/dL, and they showed a significant increase (P≤ 0.05) of serum urea in the patients without renal failure comparison with the control group. Figure (2) indicated a significant increase in serum uric acid concentration in the patients with renal failure (10.278 ± 0.162) mg/dL than the patients without renal failure (7.264 ± 0.369) mg/dL, while a significant increase in the patients without renal failure in comparing with control group.

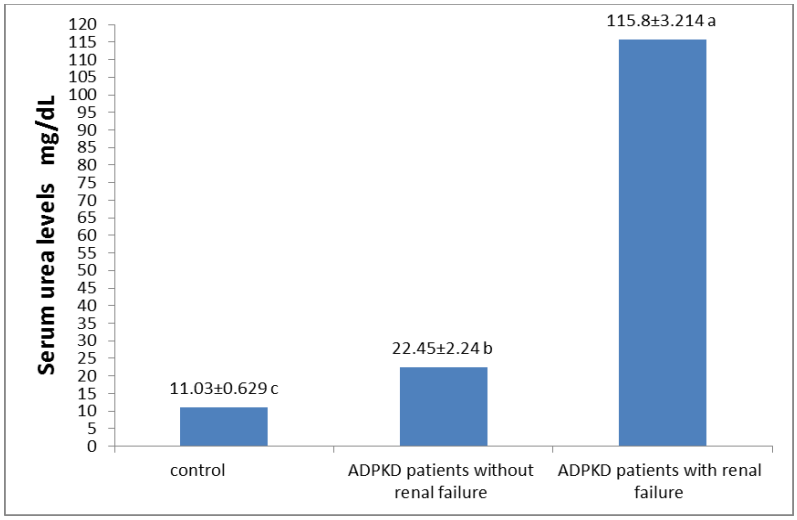

Figure (1): Serum urea levels in ADPKD patients with and without renal failure.
(**a,b,c**) : significant differences (P≤ 0.05).

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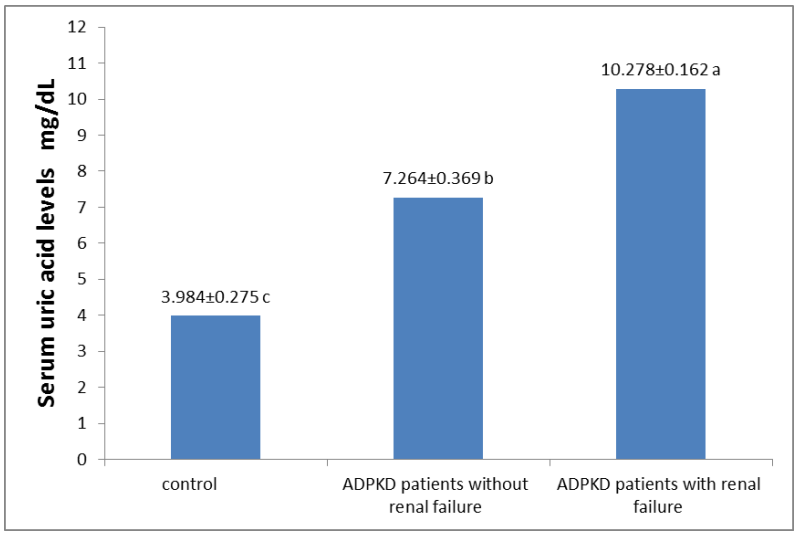

Figure (2): Serum uric acid levels in ADPKD patients with and without renal failure. (**a,b,c**): significant differences (P≤ 0.05).

Figure (3) and figure (4) are showed a significant increase (P≤0.05) in creatinine and significant decrease (P≤0.05) in albumin concentrations in the patients with renal failure (3.5 ± 0.121) mg/dL and (2.59 ± 0.343)g/dL in comparing with the patients without renal failure (1.026 ± 0.66)mg/dL and (3.803 ± 0.86)g/dL and control group (.0968 ± 0.047)mg/dL and (3.786 ± 0.134)g/dL respectively.

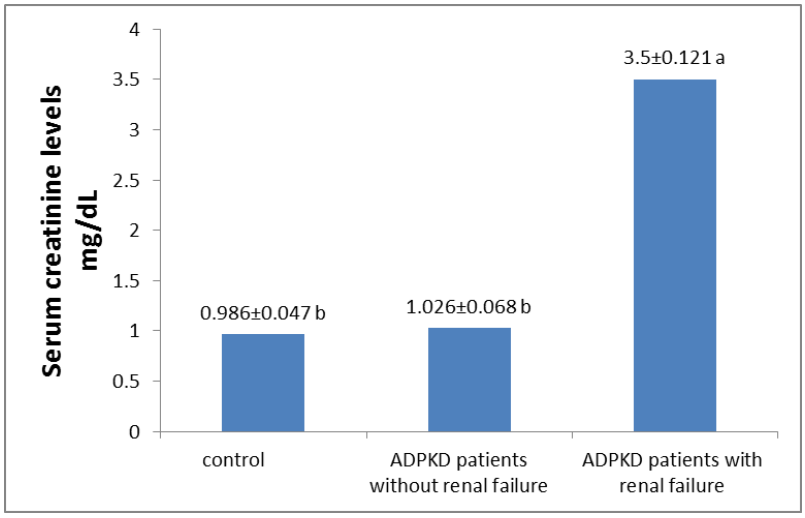

Figure (3): Serum creatinine levels in ADPKD patients with and without renal failure. (**a,b**): significant differences (P≤ 0.05).

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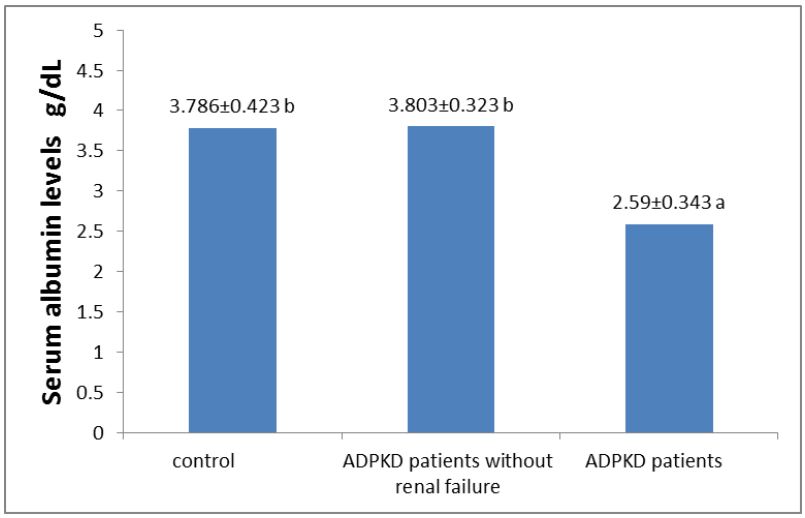

Figure (4): Serum albumin levels in ADPKD patients with and without renal failure. (a,b): significant differences (P≤ 0.05).

2. Electrolytes:

Table (2) revealed a significant increase (P≤ 0.05) in potassium ion concentration in ADPKD patients (5.466 ± 1.509) mmol/L in comparing with control group (2.34 ± 0.54) mmol/L, and a significant decrease (P≤ 0.05) in sodium ion concentration in ADPKD patients (112.017) mmol/L in comparing with control group (147.25 ± 2.303) mmol/L. Figure (5) indicated a significant increase (P≤ 0.05) in potassium ion concentration in the patients with renal failure (5.466 ±1.509) mmol/L than the patients without renal failure (6.821 ± 0.367) mmol/L. also, showed a significant difference between the patients without renal failure and control group that was (4.410 ± 0,135) mmol/L. Figure (6) revealed a significant decrease (P≤ 0.05) in sodium ion concentration in the patients with renal failure (87.06 ± 3.292) mmol/L than the patients without renal failure (129.843 ± 4.415) mmol/L. There is a significant decrease (P≤ 0.05) of sodium ion concentration in the patients without renal failure comparing with control group (147.25 ± 2.303) mmol/L.

Table (2): Electrolyte levels in the ADPKD patients and control group

Groups / Electrolyte / Criteria	Mean ±S.E.	
	Control N=10	**Patients N=24**
Potassium K+: mmol/L	2.34±0.54	5.466 ± 1.509 *
Sodium Na+: mmol/L	147.250 ± 2.303	112.017 ± 5.248 *

(*): significant difference (P≤ 0.05)

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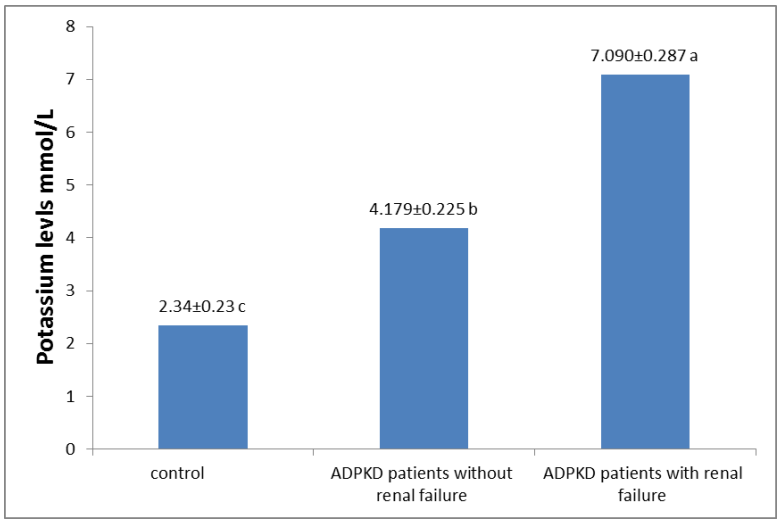

Figure (5): Potassium ion levels in ADPKD patients with and without renal failure. (a,b,c): significant differences (P<0.05).

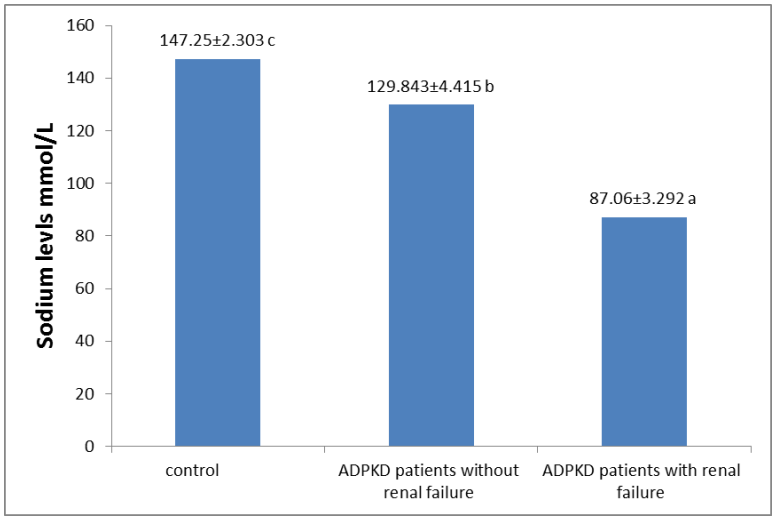

Figure (6): Sodium ion levels in ADPKD patients with and without renal failure. (a,b,c): significant differences (P≤ 0.05).

3. Liver function tests:

Table (3) showed non-significant differences (P≤ 0.05) in the liver function enzymes, ALT and AST concentrations comparing with control group.

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Table (3): Liver function enzyme leves in the ADPKD patients and control group.

Groups / Liver enzymes	Mean ±S.E.	
	Control N=10	**ADPKD Patients** N=24
AST : U/L	41.300 ± 2.660	38.880 ± 2.030 ^{ns}
ALT : U/L	18.900 ± 1.693	18.271 ± 1.122 ^{ns}

ns: non-significant ($P \leq 0.05$).

Discussion:

The final stage of renal failure is characterized by azotemia, elevated serum urea and serum creatinine resulting from a rapid decline in glomerular filtration rate (GFR) and leading to treatment by dialysis [9]. The slightly increasing of serum urea in the patients without renal failure comparing with control group, possibly due to: **1)** Non-renal factors including dietary protein intake, endogenous protein catabolism, fluid intake, and hepatic urea synthesis [10]. **2)** Medications such as antihypertensive drugs (ACE inhibitors) and diuretics [11,12]. **3)** Increase kidney damage due to both development and expansion of cysts may be causes measurable decline in kidney function, detected by a rise in urea above the physiological range [13]. Because of these overlaps above, serum urea may not be a sensitive and specific marker for the ADPKD patients without renal failure especially with the presence of a normal finding of serum creatinine level [14]. The serum uric acid concentration is determined largely by the rate of purine metabolism and the efficiency of renal clearance. Therefore, significant amounts of uric acid may accumulation in the kidney of patients approaching ESRD [15]. The clinical impact appears since uric acid has a relative insolubility, particularly in the acidic environment of the distal nephron. As a result, states of enhanced purine catabolism increase the urate load on the kidney leading to intrarenal precipitation. Any functional decline which reduces GFRs and tubular reabsorption secondarily lead to uric acid elevation [16]. The elevated serum levels of uric acid or called hyperuricemia are common in patients with kidney disease or in those receiving maintenance dialysis therapies. Higher serum uric acid levels are associated with earlier onset of hypertension, larger kidney volume and increased hazard for ESRD in patients with ADPKD [17]. Figure (3) was showed normal levels of serum creatinine in the ADPKD patients without renal failure. Torres *et al*. [18] were mentioned that most patients with ADPKD renal function is maintained within the normal range, despite relentless growth of cysts, until the fourth to sixth decade of life. Helal *et al*.[19] were found normal serum creatinine levels in young patients with ADPKD. By the time, renal function stars declining due mainly to enlargement of kidneys and cyst growth volumes [20]. In recent study found that serum albumin concentrations were normal in the ADPKD patients without renal failure. Azurmendi *et al*. [21] mentioned that the young patients with ADPKD have normal albumin

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levels. Yoo *et al*. [22] found the patients with ADPKD were have normal levels of serum albumin, and mentioned may be healthy diet, which taken by these patients, or because they did not suffer from proteinuria.

The results indicated the presence of hyperkalemia in the patients with ADPKD (table 2 and figure 5), may be due to impaired renal function and/or medications such as antihypertension and diuretics. An *et al*. [23] mentioned that drug therapy and impaired renal function are the main factors predisposing to the development of hyperkalemia. Veeramuthumari and Isabel [24] found increase levels of serum potassium in patients with ADPKD at different ages and all the disease stages. Hyperkalemia is common in patients with ESRD and is a leading indication for emergency dialysis among patients treated with chronic hemodialysis [25]. The most common antihypertensive drugs which caused of hyperkalemia are angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), while diuretics which causing of that are Potassium-sparing diuretics (amiloride and triamterene). These medications almost always received by the patients with ADPKD [26,27]. The results indicated the presence of hyponatremia in the patients with ADPKD (table 2 and figure 6). Patients with chronic kidney disease (CKD) may be more susceptible to the development of dysnatremias by virtue of their diminished ability to maintain water homeostasis in the face of decreasing kidney function [28]. Veeramuthumari and Isabel [24] were found that the patients with ADPKD have deceased serum sodium levels which reached 98.88± 1.38 mmol/L. With advancing CKD, the kidney has a remarkable ability to maintain hemostasis, regulation of water imbalance. Therefore, the prevalence of hyponatremia in patients with renal replacement therapy is common, as well as other reason is that fluid and electrolytes balance in these patients dependent on non-renal routes [29]. The important causes of hyponatremia are medications. On of important drugs are diuretics, which affected sodium and water hemostasis for example thiazide or thiazide-like agents. Antihypertensive drugs such as ACE inhibitors, also involved with decreasing of sodium [30,28]. The recent study showed the presence of normal concentrations of both enzymes in the patients with ADPKD, may be a sign that the liver function was unaffected in these patients. Oreopoulos *et al*. [31] found the liver function tests were normal in all patients with ADPKD. Torres *et al*. [32] found that all tests of the liver function in most patients with ADPKD were normal. Chauveau *et al*. [33] stated, although progressive deterioration of renal function over decades in the ADPKD patients, hepatic function remains unaffected. Also Tasci *et al*. [34] found the AST and ALT levels were normal in patient with ADPKD.

Conclusion:

It is very important, screening and regular monitoring of kidney function criteria for patients with disease so as to avoid disease complications prematurely. Doctors should attention the quality of medicines given to kidney patients, especially antihypertensives and diuretics. Monitoring, the levels of electrolytes in these patients, is also important.

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