

## Study of some physiological parameters in renal failure patients

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### دراسة بعض المعايير الفسلجية في مرضى الفشل الكلوي

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### المستخلص

الفشل الكلوي يشير الى الظروف التي تفقد بها الكلية وظائفها الطبيعية . الديليزة هي احد الاستراتيجيات الشائعة لعلاج استبدال الكلية . تهدف الدراسة الحالية الى دراسة بعض المعايير الفسلجية في مرضى الفشل الكلوي قبل وبعد الديليزة ومقارنة النتائج مع مجموعة السيطرة. شملت الدراسة 134 مريض (94 يعانون الغسيل الدموي , (52 رجل و(42 امرأة , (40 مريض يعانون الغسيل البريتوني , (24 رجل و(16 امرأة. بينما كانت عينة السيطرة (57 شخص (29 رجل و(28 امرأة. اظهرت النتائج زيادة معنوية ( $P < 0.01$ ) في اليوريا والكرياتينين وهرمون الالدوستيرون في رجال ونساء الغسيل الدموي والبريتوني مقارنة مع مجموعة السيطرة في حين أظهرت انخفاضاً معنوياً ( $P < 0.01$ ) في الكالسيوم والبروتين وهرمون الاريتروبايوتين وفعالية الخلايا البلعية في رجال ونساء الغسيل الدموي والبريتوني مقارنة مع مجموعة السيطرة .

### Abstract

Renal failure refers to a condition where the kidneys lose their normal functionality. Dialysis is one of the most common strategy of renal replacement therapy . The aims of the study is to study of some physiological paramerters in patients with renal failure before and after dialysis and compared the results with healthy people. ( 134 ) patients were taken for this study, 94 patients undergoing hemodialysis, 52 males and 42 females, 40 patients undergoing peritoneal dialysis, 24 males and 16 females .The subjects of control group were 57 individuals 29 males and 28 females. The present results showed that there is significant increase ( $P < 0.01$ ) in urea , creatinine and aldosterone in males, female hemodialysis and peritoneal dialysis patients compared to control . While there were significant decrease ( $P < 0.01$ ) in total protein ,calcium , erythropoietin and phagocytic activity compared to control but there was no significant difference between before and after dialysis.

### Introduction

Renal failure refers to a condition where the kidneys lose their normal functionality, which may be due to various factors including infections, autoimmune diseases, diabetes, endocrine disorders, cancer, and toxic chemicals (1). Renal failure occurs when a sufficient number of nephrons are damaged and therefore the kidneys unable to perform their functions, it can be divided into two main types, namely acute and chronic renal failure (2,3). Acute renal failure (ARF) is a common condition in hospitalized patients, characterized by a rapid fall in glomerular filtration rate (GFR), carries a high morbidity and

mortality, often preventable, so rapid recognition and treatment may prevent irreversible loss of nephrons. (4). Chronic renal failure (CRF) is growing among all population groups worldwide and the incidence of end-stage renal disease (ESRD) continues to increase (5). CRF is defined as kidney damage for more than three months as evidenced by structural or functional abnormalities with or without decreased glomerular filtration rate (GFR) and manifested either as pathological abnormalities or kidney damage markers in blood or urine or in the imaging test, many people are unaware of the problem until more than 70% of kidney function has been lost (6,7). It is a major public health problem, with increasing incidence and prevalence, poor outcomes, and high costs. which without renal replacement therapy would lead to death (8,9). Dialysis (hemo- and peritoneal) is regarded one of the most common strategy of renal replacement therapy and the main sole for saving the life (10). It is defined as a procedure that removes excess fluids and toxic end products of metabolism such as urea from the plasma and corrects electrolytes balance by dialyzing the patients' blood against fluid containing no urea but with appropriate concentrations of electrolytes free ionized calcium and other plasma constituents (11). It can be divided into two classes: hemodialysis and peritoneal dialysis. Hemodialysis (HD) is a renal replacement therapy; the treatment process in HD consists of circulating the patient's blood through an artificial kidney, a dialyser, to remove waste products, such as potassium, urea, and excess fluids (12). It relies on the principle of solute diffusion across a semi permeable membrane movement of metabolic waste products takes place down a concentration gradient from the circulation in to the dialysate, and in the reverse direction (13). Peritoneal dialysis is the method of treatment of terminal-stage chronic kidney failure. Till now, this method is complementary to haemodialysis. It is based on the principles of the diffusion of solutes and ultrafiltration of fluids across the peritoneal membrane, which acts as a filter. The dialysate is introduced into the peritoneum via the previously positioned peritoneal catheter. The peritoneal dialysis is carried out on daily basis, at home by the patient, and the "exchange" is repeated 4-5 times during the 24 hour (14). The aims of the study are to study of renal function, biochemical, hormonal and phagocytic activity in patients with renal failure before and after dialysis and compared the results with healthy people.

## **Material and methods**

### **Patients and control subjects**

The subjects for this study consist of patients undergoing with renal failure in the unit of artificial kidney in AL-Kut Hospital in AL-Kut city, Wasit Province, Iraq; during the period from November, 2012 to March, 2013. one hundred thirty four patients were taken for this study. The patients in this study were divided into two groups according to the type of dialysis: 94 patients undergoing hemodialysis, 52 males with age range (21-69) years and 42 females with age range (21-70) years, 40 patients undergoing peritoneal dialysis, 24 males with age range (23-60) years and 16 females with age range (18-63) years. Blood samples were collected from patients and the history was taken from patients and their parents including: name, age, sex, type of dialysis, family history of renal failure. The subjects of control group in current study were 57 individuals non-undergoing renal failure who were free from any signs and symptoms of chronic renal disease, liver disease, lipid disorders, diabetes mellitus, hypertension and other. 29 males with age range (20-43) years and 28 females with age range (21-43) years used as control.

## Blood samples

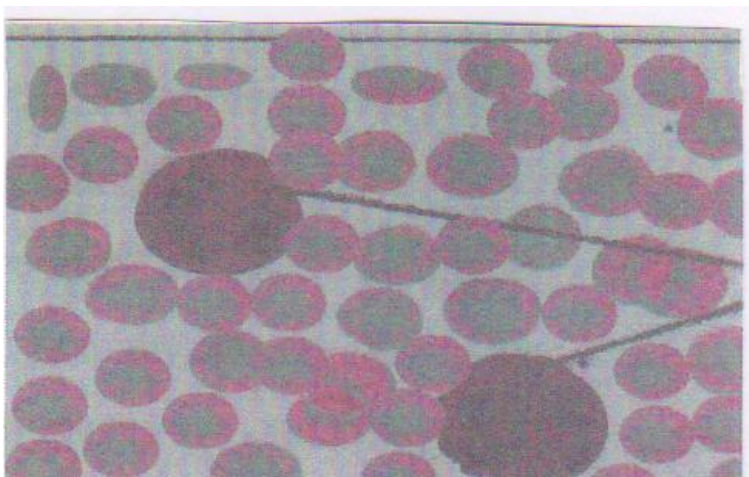
Eight milliliters of venous blood were drawn from control subjects and patients with renal failure by using disposable syringe of 10 ml before and after dialysis process, one ml for nitroblue tetrazolium stain ( N.B.T. stain) , remaining seven ml of blood samples was put in disposable plane tubes, left at room temperature for 30 minutes for clot formation and then centrifuged for 10 minutes at 3000 run per minute transferred immediately into another tube and frozen at (-20 C) for subsequent analysis The serum was separated and divided into three parts and kept in the eppendorf tube which is used to analyze of biochemical tests (serum creatinin, blood urea ,calcium and total protein ) and used for estimation of serum Aldosterone and Erythropieotin hormones.

## Biochemical tests

To evaluate each one of the biochemical parameters (Serum Creatinine and Blood Urea ), used Reflotron Kit specific for each parameter by Roche Diagnostic GmbH , for assay total protein and calicum we used Spectrophotometer Instrument and ELISA for aldosterone and erythropoietin assay .

## Nitroblue-Tetrazolium stain (NBT) reduction by neutrophils

The Nitroblue Tetrazolium (NBT) stain reduction is regarded as an index of the superoxide ion production. The quantity of reduced NBT , Formosan which accumulates in the cells , is correlated to its phagocytic activity, The semi-quantities NBT reduction was studied according to the method of Nypjrk (15) .



**Figure (1): Nitro blue Tetrazolium reduction by neutrophils**

## Statistical analysis

The data of present study was made with using Genstat Program and analyzed by ANOVA (one way analysis).. LSD was used for comparisons between the haemodialysis, peritoneal dialysis patients and control group and between before and after dialysis.  $P < 0.01$  was considered to be statistically significant.

## Results

The results in Table (1) show that there are significant increase ( $P < 0.01$ ) in the mean values of urea and creatinine in males hemodialysis and peritoneal dialysis patients compared to control and there are significant decrease ( $P < 0.01$ ) in urea and creatinine after dialysis compared to before dialysis. While there is significant decrease ( $P < 0.01$ ) in the mean values of serum total protein and serum calcium before dialysis compared to control but no significant difference between after dialysis and control and there is significant decrease ( $P < 0.01$ ) in the mean value of erythropoietin compared with control but no significant difference between before and after dialysis. While there is significant increase ( $P < 0.01$ ) in the mean values of aldosterone compared to control and no significant difference between before and after dialysis. The results in Table (2) show that there are significant increase ( $P < 0.01$ ) in the mean values of urea and creatinine in females hemodialysis and peritoneal dialysis patients compared to control and there is significant decrease ( $P < 0.01$ ) in urea and creatinine after dialysis compared to before dialysis. While that there are significant decrease ( $P < 0.01$ ) in the mean value of calcium and serum total protein before dialysis compared to control but no significant difference between after dialysis and control and that there is significant decrease ( $P < 0.01$ ) in the mean value of erythropoietin in females hemodialysis and peritoneal dialysis patients compared with control but no significant difference between before and after dialysis. While there is significant increase ( $P < 0.01$ ) in the mean values of aldosterone compared to control and shows that there is no significant difference between before and after dialysis. The results in Table (3) shows that there is significant decrease ( $P < 0.01$ ) in the mean value of neutrophil activity in males hemodialysis and Peritoneal dialysis patients compared with control but there is no significant difference between males hemodialysis and Peritoneal dialysis patients. The results in Table (4) shows that there is significant decrease ( $P < 0.01$ ) in the mean value of neutrophil activity in females hemodialysis and Peritoneal dialysis patients compared with control but there is no significant difference between females hemodialysis and Peritoneal dialysis patient.

**Table ( 1 ): The mean value of the biochemical and hormonal parameters in the male hemodialysis and peritoneal dialysis**

Parameter Type Of Dialysis		Urea (mg/dl)	Creatin ine (mg/dl)	Total protein (g/dl)	Calicum (mg/dl)	EPO Pg /ml	ALD Pg /ml
Control		29.7 a	0.59 a	6.07 a	5.91 a	26.77 a	243.2 a
Hemodialysis	before	158.2 b	9.03 b	5.56 b	4.47 b	13.46 b	351.5 b
	after	75.2 c	5.15 c	6.47 a	6.46 a	12.15 b	350.1 b
peritonal	before	227.8 b	9.65 b	5.15 a	4.28 a	12.38 b	340.4 b
	after	58.4 c	3.54 c	7.34 a	6.74 a	10.96 b	347.5 b

\*The different captile letter refers to the significant differences (  $P < 0.01$  ) between vertical value

**Table ( 2 ) : The mean value of the biochemical and hormonal parameters in the females hemodialysis and peritoneal dialysis**

Parameter Type Of Dialysis		Urea (mg / dl)	Creatinine (mg /dl )	Total protein (g/dl)	Calicum (mg/dl)	EPO Pg /ml	ALD Pg /ml
Control		31.1 a	0.69 a	5.92 a	5.66 a	24.89 a	241.0 a
Hemodialysis	before	153.0 b	7.90 b	5.81 b	6.77 b	13.12 b	338.7 b
	after	69.6 c	4.51 c	6.74 c	7.11 c	11.88 b	344.5 b
peritoneal	before	214.0 b	8.93 b	6.20 b	5.99 b	11.21 b	355.6 b
	after	50.9 c	3.17 c	5.92 a	6.72 a	9.87 b	354.4 b

\*The different captile letter refers to the significant differences  $P < 0.01$  between vertical value

**Table ( 3 ): Neutrophil activity by using Nitroblue Tetrazolium stain of males hemodialysis and Peritoneal dialysis**

<b>Group Males Hemodialysis and Peritoneal dialysis</b>			
<b>Parameter</b>	<b>Control n=29</b>	<b>Hemodialysis n=52</b>	<b>Peritoneal dialysis n=24</b>
		<b>before dialysis</b>	<b>before dialysis</b>
<b>Neutrophil Activity %</b>	15.04 a	7.48 b	7.37 b

\*The different captile letter refers to the significant differences  $P < 0.01$  between horizontal value

**Table (4): Neutrophil activity by using Nitroblue Tetrazolium stain of females hemodialysis and Peritoneal dialysis**

<b>Group Females Hemodialysis and Peritoneal dialysis</b>			
<b>Parameter</b>	<b>Control n=28</b>	<b>Hemodialysis n=42</b>	<b>Peritoneal dialysis n=16</b>
		<b>before dialysis</b>	<b>before dialysis</b>
<b>Neutrophil Activity %</b>	13.31 a	8.15 b	8.75 b

\*The different captile letter refers to the significant differences  $P < 0.01$  between horizontal value

## Discussion

### The biochemical test

This study shows that blood urea and creatinine increase in patients of renal failure ( hemodialysis and peritoneal dialysis ) in both sex (males and females) before and after dialysis compared to the control groups, these results agreed with (16) who showed significant increase in urea, creatinine concentrations in chronic kidney disease. Also,(17) observed that serum creatinine increased in patients with chronic renal failure and it is widely interpreted as a measure only of renal function. Similarly, (1) and (18) agreed with our study these studies concluded that urea and creatinine are quantitatively the most important solute excreted by the kidney and it was the first organic solute detected in the blood of patients with CRF . This increase in urea and creatinine level occurs because in CRF the kidney lose its ability to eliminate nitrogenous wastes from the blood results in accumulation of these substances in the blood (19). In our study the parameters of (urea and creatinine) showed significant decrease after dialysis in the males and females of renal failure ( hemodialysis and peritoneal dialysis ) this result is agreed to study with (18) because treatment with dialysis in both type remove toxins from the blood where the blood of the patient is continuously being withdrawn dialyzer and returned to the patient (20). When comparing the mean value of urea before dialysis in males and females hemodialysis and peritoneal dialysis showed significant difference were found But shows no significant in the mean value of creatinine before dialysis in males and females hemodialysis and peritoneal dialysis. While when comparing the mean value of urea and creatinine after dialysis in males and females hemodialysis and peritoneal dialysis showed significant difference were found. In this study the mean values of total protein decrease in patients of renal failure ( hemodialysis and peritoneal dialysis ) in both sex (males and females) before dialysis compared to the control groups, these results agreed with (21) who showed that proteinuria is the most common finding in renal failure patients. Also (22) reported that nephrotic syndrome is defined as urine total protein excretion greater than 3.5 g/dl or total protein– creatinine ratio greater than 3.5 g/g, low serum albumin level, and peripheral edema. The observed decrease in serum total protein concentration in renal failure patients may be due to proteinuria, which are the most key finding differentiating edematous states caused by kidney disease from other diseases (23) .The result show that the mean value of total protein before dialysis increase when comparing to before dialysis because haemoconcentration following dialysis procedure and metabolic acidosis which increase whole body protein degradation (24). Our study , shows that the mean values of calcium decrease in patients of renal failure ( hemodialysis and peritoneal dialysis ) in both sex (males and females) before dialysis compared to the control groups, these results agreed with (25) who observed an algorithm to start calcium infusion when a steep fall in calcium levels. However, it might be better to prevent hypocalcemia altogether. Also,(26) reported the role of calcitriol to control hypocalcemia after parathyroidectomy in chronic kidney disease. chronic renal insufficiency is associated with hyperphosphatemia, the elevated serum phosphate levels directly depress serum calcium levels and thereby stimulate parathyroid gland activity, secondary hyperparathyroidism is caused by any condition associated with a chronic depression in the serum calcium level, because low serum calcium leads to compensatory over activity of the parathyroids, so renal failure is by far the most common cause of secondary hyperparathyroidism (27). When comparing the mean value of total protein and calcium before and after dialysis in males and females hemodialysis and peritoneal dialysis showed no significant difference were found.



## The hormonal test

This study shows that the mean value of erythropoietin decrease in patients of renal failure ( hemodialysis and peritoneal dialysis ) in both sex (males and females) before and after dialysis compared to the control groups, these results agreed with study by (28) .These finding could explained as anemia first appears when the GFR falls below 40 ml/minute, and is present in most patients with ESRD because in renal failure, erythropoietin production usually is insufficient to stimulate adequate red blood cell production by the bone marrow,Also (29) show that it is well recognized that patients with chronic kidney disease have low hemoglobin levels and the etiology of the anemia was eventually determined to be primarily due to the reduction of erythropoietin production and activity .Similary (30) who reported that chronic renal failure leads to hyporegenerative anemia due to erythropoietin deficiency,the creatinine clearance and hemoglobin levels, at which anemia treatment with recombinant erythropoietin should be started, are unclear. Interpretation of serum erythropoietin levels in the context of renal insufficiency remains controversial.. In our study , The mean value of aldosterone increase in patients of renal failure ( hemodialysis and peritoneal dialysis ) in both sex (males and females) before and after dialysis compared to the control groups, these results agreed with study by (31) who reported that several clinical investigations identified increased aldosterone levels in renal failure. Recent evidence also implicates aldosterone as an important pathogenetic factor in progressive renal disease (32). When comparing the mean value of erythropoietin and aldosterone in the male and female hemodialysis and peritoneal dialysis before and after dialysis there is no significant difference were found.

## Discussion of neutrophil activity by using Nitroblue Tetrazolium stain ( NBT )

In our study, Neutrophil activity showed significant decrease in both type ( hemodialysis and peritoneal dialysis ) in both sex (males and females) patients before dialysis compared to the control groups .These results agreed with study by (33) who reported that Patients with renal failure are highly susceptible to infection, in part because uremia decreases the killing capacity of phagocytic leucocytes. , Similary (34) observed that the functional impairment described in uremic neutrophils is therefore mainly a result of their reduced ability to kill microorganisms intracellularly and is believed to increase the susceptibility to infections . Also (35) who show that there is a significant decrease in the phagocytic activity of neutrophils was observed in the both dialysed groups. As neutrophils play a crucial role in host defence against bacterial and fungal infections, neutrophil functions such as the production of reactive oxygen species (ROS) or phagocytosis have been studied extensively. This is especially true for patients undergoing dialysis for end-stage renal disease because infection is one of the leading causes of morbidity and mortality in these patients. In this context functional impairment of neutrophils in uraemia is believed to increase the susceptibility to infections (36). Neutrophils are the cellular hallmark of acute inflammation and rapidly accumulate in large numbers at sites of infection. During their short life span (hours to days) neutrophils perform many functions of host defense, including phagocytosis and killing of bacteria with reactive oxygen intermediates and other mechanisms. Although neutrophils have been viewed primarily in terms of their contributions to innate immunity, they also have the ability to influence adaptive immunity (37). Among patients with defects of the phagocytic component of the immune system, renal failure patients are highly susceptible to infection characterized by high morbidity and mortality, related to an impairment of the phagocytic response (38) . Neutrophils play an important role in non-specific immune response and organism resistance, specifically in anti-bacterial resistance as effectors, inducing and regulating cells. They reveal many features which are crucial in organism

immunity: to produce and adhere towards vascular endothelial cells, migrate to inflammatory sites through the vessel walls, recognize and phagocytize opsonized molecules, and degrade and release proteins from granules (39). Chronic renal failure causes secondary immunosuppression, this is well documented in human, where infections are still a major cause of morbidity and mortality in end-stage renal disease patients, there are many reports of neutrophil dysfunction and increased risk of infection in these patients (40). The mechanisms responsible for reduced neutrophil functions are not well understood and have been attributed to iron overload, zinc deficiency, increased intracellular ionized calcium, anaemia, malnutrition, short time on dialysis and dialysis therapy (41) and (36). When comparing the result of phagocytic activity in the male and female hemodialysis and peritoneal dialysis there is no significant difference were found. These results agreed with study by (42) observed that the both type of dialysis patients are weak in immune host defense, which is associated with their high morbidity of infection.

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