

## Determination of Several Biochemical Markers in Sera of Patients with Kidney Diseases

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### Abstract

Renal failure is a medical condition from which the kidneys fail to adequately filter toxins and waste products from the blood. Renal failure is described as a decrease in the glomerular filtration rate. Biochemically, renal failure is typically detected by an elevated serum creatinine level. Problems frequently encountered in kidney malfunction include abnormal fluid levels in the body, deranged acid levels, abnormal levels of potassium, calcium, phosphate, and (in the longer term) anemia as well as delayed healing in broken bones. Depending on the cause, hematuria and proteinuria may occur. Long-term kidney problems have significant repercussions on other diseases, such as cardiovascular disease. The present study aim to evaluate several biochemical markers in Patients with Kidney Diseases and effect of these parameters in development the disease. Laboratory investigations including Renal function tests (RFT), fasting blood glucose, S. calcium, total protein, Uric acid, S. potassium, S. Sodium, and (MDA) as lipid peroxidation biomarker, gonadal Harmony had been measured in male and female with renal failure. Blood samples were obtained from the patients and matching group of healthy volunteer subjects were considered as control group who came to the Al-Yarmok hospital for health checkup. There were significant difference in fasting blood glucose, Serum urea ,creatinine, S. calcium, S.sodium, MDA and uric acid in the patients when compared to control group. MDA showed significantly increased between men and women groups ( $P < 0.01$ ). There was a negative correlation between MDA [ $\mu$  mol/L] with Potassium [mg/dl/] ( $r = 0.63$ ,  $p < 0.091$ ), and MDA with calcium [mg/dl/] ( $r = 0.58$ ,  $p < 0.019$ ), respectively in patients group while no correlation was found among control subjects. MDA may play a role in development the kidney disease so more study may be need to stady MDA and another antioxidant to determine effect of them in the kidney disease.

Keywords: renal failure , Malondialdehyde, uric acid, sex hormones.

### Introduction

Renal failure occurs when the kidneys are unable to do their job: to filter wastes from the blood, help regulate blood pressure, and regulate salt and water balances in the body. As blood flows through the kidneys, it is filtered, and wastes are removed and sent to the bladder as urine. If kidney function becomes impaired, acute (rapid) or chronic (gradually developing) renal failure may occur. With acute renal failure, kidney function can return to normal if the underlying cause of the failure is discovered and successfully treated [1,2].

Uric acid is strongly associated with renal failure and cardiovascular disease [3,4] and is particularly common in people with hypertension, metabolic syndrome, and associated with its metabolic abnormalities [5-8]. Leading to the suggestion that this should promote initial kidney damage or its

Progression[9]. Urea is produced as a break down product of protein. Urea clearance grossly underestimates glomerular filtration rate GFR. In addition, the amount of urea reabsorbed increases with dehydration [10].

Creatinine is a metabolic substance product from muscle metabolism (it is derived from creatine and phosphocreatine). For the majority of patients the muscle turnover varies little from day to day, and the serum creatinine is more or less constant. Creatinine is filtered and excreted by the kidney. Serum creatinine is probably the most widely used indirect measure of glomerular filtration rate GFR [11].

Malondialdehyde (MDA) has been widely used as an indicator of oxidative stress and lipid peroxidation [12,13]. Renal failure patients are also subjected to enhanced oxidative stress due to reduced antioxidant systems and increased pro oxidant

activity[14,15]. During this process polyunsaturated fatty acids, present in cell membrane are oxidized in vivo to form aldehydes of variable chain length like MDA. This lipid peroxidation product can structurally alter DNA, RNA, body protein and other biomolecules.[16].

Luteinizing hormone (LH, also known as lutropin) is a hormone produced by the anterior pituitary gland. In females, an acute rise of LH called the LH surge triggers ovulation and development of the corpus luteum. In males, where LH had also been called interstitial cell-stimulating hormone (ICSH), it stimulates Leydig cell production of testosterone, it acts synergistically with FSH. The FSH is a hormone found in humans and other animals. It is synthesized and secreted by gonadotrophs of the anterior pituitary gland. FSH regulates the development, growth, pubertal maturation, and reproductive processes of the body. FSH and LH act synergistically in reproduction [17]. Sexual dysfunction is a set of disorders characterized by physical and psychologic changes that result in the inability to perform satisfactory sexual activities. The condition has been found to be significantly more common in men and women with chronic kidney disease (CKD) than in the general population [18]. gonadal failure is an important consequence of chronic renal failure. The finding that LH levels are typically increased is consistent with the presence of testicular damage. However, the lack of Leydig cell hypertrophy and normal estradiol level also raise the possibility of functional hypogonadism [19].

### Aim of Study

The present study aim to evaluate several biochemical markers in Patients with Kidney Diseases and effect of these parameters in development the disease.

### Materials and Methods

A Five ml of blood serum had been collected from each subject by vein puncture, centrifuged at 3000 rpm for 5 min after clotting at room temperature. Thirty patients had been obtained from renal failure [16 males age (32-60) years ( $M \pm SD$ :  $41.56 \pm 10.46$ )] and [14 females age (33-63) years ( $M \pm SD$ :  $42.14 \pm$

9.78)]. The patients were diagnosed by specialist doctors in AL-Yarmok hospital. Twenty healthy subjects [10 males age (32-52) years ( $M \pm SD$ :  $39.5 \pm 6.50$ )] and [10 females age (34-49) years ( $M \pm SD$ :  $38.9 \pm 4.33$ )]. All patients were questioned some information like history taking, thorough clinical examination, and laboratory investigations including kidney function, the level of lipid peroxidation expressed as MDA, uric acid, fasting blood sugar and total protein were measured by spectrophotometric methods supplied by Randox Diagnostic. The MDA levels were measured by the double heating method [20]. The principle of the method was based on the spectrophotometric measurement of the colour developed during the reaction of thiobarbituric acid with MDA. The concentration of thiobarbituric acid reactive substances was calculated by the absorbance coefficient of malondialdehydethiobarbituric acid complex. LH and FSH were measured by Enzyme Linked Immunosorbent Assay (ELISA) (Biovender Laboratory Medicine, Brno, Czech Republic).

Statistical analyses of this study were performed using SPSS version 15.0 for Windows (Statistical Package for Social Science, Inc., Chicago, IL, USA). Descriptive analysis was used to show the mean and standard deviation of variables. The significance of difference between mean values was estimated by Student T-Test. The probability  $P < 0.05$  = significant,  $P > 0.05$  = non-significant. Correlation analysis was used to test the linear relationship between parameters. ANOVA test was used to show the differences between variables of differentiated groups.

### Results and Discussion

There is no significant different in age between patient and control group. Fasting blood glucose, Urea, Creatinine, Serum levels Sodium and MDA were found to be significantly increase with P value  $< 0.001$ , Uric acid was found to be significantly increase with P value  $< 0.05$ . There were no significant difference [P value  $> 0.05$ ] between patient and control levels of serum potassium, total protein, LH, and FSH as shown in Table (1). There was a significant decreased in serum level in calcium level in patient when compared to control group as shown in Table (1).

**Table (1)**

**The mean and standard deviation of Age, FBG, Urea, Creatinine, Uric acid, Calcium, Potassium, Sodium, MDA, Total protein, LH and FSH in patients group and control group.**

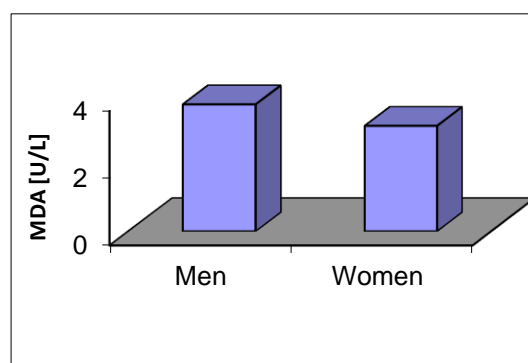
Characteristic	Patients [mean±SD] [n=30]	Control [mean±S] [n=20]	PVale
Age year	41.36±9.98	39.20±5.38	N.S
FBG[mg/dl]	129.33±30.66	94.50±11.22	<0.001
Urea[mg/dl]	116.03±36.84	31.00±4.82	<0.001
Creatinine[mg/l]	5.53±2.23	0.92±0.05	<0.001
Uric acid[mg/dl]	6.09 ± 1.58	4.91 ± 1.05	<0.05
S.Calcium[mg/dl/]	8.26±1.01	9.63±0.71	<0.01
S.Potassi[mg/dl/]	4.43±0.71	4.86±0.28	N.S
S.Sodium[mEq/L]	137.50±4.93	151.6±3.88	<0.001
MDA [U/L]	3.44±0.59	1.41±1.16	<0.001
Total prote[gm/dl]	5.86± 0.89	6.09± 0.63	N.S
LH [U/L]	13.04±8.44	12.91±13.79	N.S
FSH[U/L]	10.96±9.46	10.35±5.45	N.S

MDA is a lipid peroxidation product which is formed during oxidation process of PUFA by reactive oxygen species. MDA is the sensitive marker of lipid peroxidation [21]. Present results are in agreement with the group's mentioned in that the serum level of MDA of haemodialysis patients is significantly increased from that of control [22-24], although hemodialysis leads to improvement of several bio-chemical parameters like creatinine, urea levels and plasma lipid patterns, but it can cause harmful atherogenic effects. The increase in lipid peroxidation resulting from hemodialysis could be provoked by bio incompatibility of dialysis membrane. When cells come in contact with the dialyzer membrane leads to sensitization of cell membrane components leading to compliment activation which cause formation of other reactive oxygen species which will initiate peroxidation of PUFA. [25], This situation probably in due to direct relation between the blood of haemodialysis patients with dialysis instrument which is a conductive factor in oxidative stress and subsequent increased production of free radicals in haemodialysis patient. The probable

oxidative destruction can be due to increasing production of free radicals [26].

In the present study serum FSH, LH levels N.S significant differences compared to the reference group. Another study who proved that mean progesterone and FSH levels in patients were not significantly different from those of control subjects [27].

MDA showed significant in men compared to women in patients group, while there was no significant different between them in control group (P<0.01). There was no significant different was observe with Age, FBG, Urea, Creatinine, Calcium, Potassium, Sodium and total protein in the men group when compared with women group.



**Fig.(1) Comparison of MDA in man and women in patients group.**

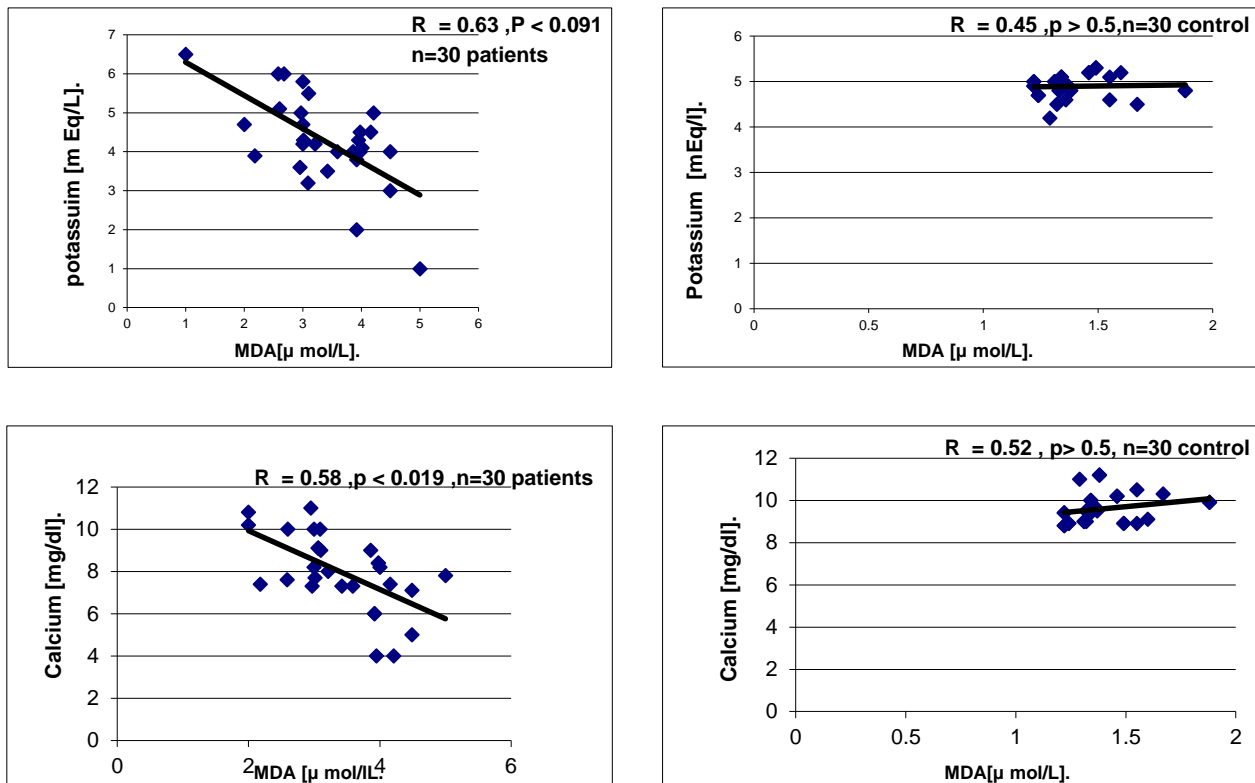
The results showed a significant different in mean of serum MDA between men and women in patients group, while there was no significant different between them in control group (P<0.01). There was no significant different was observe with Age, FBG, Urea, Creatinine, Calcium, Potassium, Sodium and total protein in the men group when compared with women group.

The MDA levels were higher in male than in female in patients, this finding agrees with other study [28]. Who conclude that there is some information on oxidative stress in men showing a pro oxidant effect of testosterone [29], in female decreased superoxide anion production by the endothelium in response to estrogen is considered contribute to vascular protective properties of estrogen [30]. MDA, a by-product of lipid per-oxidation is said to be involved in nucleic acid adduct formation which are believed to be responsible for carcinogenesis and many diseases 21. Lower

MDA levels in serum in women than men due to known protective role of female reproductive hormone against lipid peroxidation [31-32].

In this study, a significantly negative association was observed between MDA [ $\mu\text{mol/L}$ ] with Potassium [ $\text{mg/dl}$ ] ( $r=-0.63$ ,

$p<0.091$ ), Calcium [ $\text{mg/dl}$ ] ( $r=-0.58$ ,  $p<0.019$ ), while there was no significant correlation was observed in the control group as shown in Fig.(2). This shows that decrease in calcium and Potassium level causes increase in the oxidative stress.



**Fig.(2) Correlation between MDA with Potassium and Calcium in Renal failure patients and Control.**

In conclusion, a significant increase in MDA level was found in patients with renal failure. This increased was correlated significantly with serum calcium and potassium. These parameters may be useful in designing clinical studies that target utilizing antioxidant systems to provide protective pathways on the pathogenesis of renal failure.

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و FSH و MDA. لوحظ وجود زيادة مقبولة احصائيا في مستوى سكر الدم الصيامي و urea و creatinine و calcium و sodium و acid Uric و MDA عند المصابين عند مقارنتها بالاصحاء. MDA اظهر زيادة مقبولة احصائيا بين النساء والرجال المصابين ( $P < 0.01$ ). وقد اشارت الدراسة الى وجود علاقة خطية عكسية مقبولة احصائيا بين MDA و potassium ( $r = 0.63, p < 0.091$ ) و calcium ( $r=0.58, p < 0.019$ ) للمرضى، بينما لاوجود لهذه العلاقة عند الاصحاء. انزيم MDA يلعب دورا هاما في مضاعفات امراض الكلية لذي نحتاج الى دراسات اوسع لمعرفة تاثير MDA و مضادات الاكسدة في تطور حدوث المرض

### الخلاصة

الفشل الكلوي هو حالة عدم قدرة الكلى على تصفية السموم والفضلات من الدم. يوصف الفشل الكلوي بانخفاض في معدل الترشيح الكبيبي. يتم الكشف عن الفشل الكلوي عن طريق ارتفاع مستوى الكرياتينين في الدم واختلال في مستوى السوائل والحامضية والكالسيوم والبوتاسيوم والفسفور في الجسم وحيانا تاخر التئام العظام المكسورة ، وقد يحدث فقدان الدم والبروتين في البول وهناك مشاكل اخرى على المدى الطويل يكون لها انعكاسات كبيرة على امراض اخرى مثل القلب والاعوية الدموية. تهدف الدراسة الحالية تقدير عدة عوامل كيميائية حياتية في المرضى المصابين بالفشل الكلوي، واثر هذه العوامل في تطوير هذا المرض. في هذه الدراسة تم قياس مستوى سكر الدم الصيامي عند ٣٠ مريض مصاب بالفشل الكلوي، و ٢٠ شخص سليم كمجموعة ضابطة وكذلك تم قياس urea و creatinine و calcium و total protein و Uricacid و potassium و Sodium و LH