

## Role of Adrenaline and nor-adrenaline as a markers in end stage renal failure

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### Abstract

Renal failure is described as a decrease in glomerular filtration rate. Biochemically, renal failure is typically detected by an elevated serum creatinine level. Epinephrine, Nor epinephrine, a catecholamine with multiple roles including as a hormone and a neurotransmitter. The present study is aimed to early change epinephrine and nor epinephrine levels as markers in end stage renal failure. This study represents a case control study conducted on 60 end stage renal failure patient of both sexes (74% were male and (26% ) were female in age range from 1 to 30 years (mean 17.9), which carried out during the period from April 2012 to August 2012 in Tikrit Teaching Hospital in renal hemodialysis unit in Tikrit city. Blood samples were obtain from all patients before dialysis put directly into disposable tube with EDTA to get plasma to test epinephrine and nor epinephrine and anther (2ml) put directly into disposable plain tube for blood urea and serum creatine tests. All patients were send for epinephrine and norepinephrine after dialysis. The same investigations were done to the control group with nearly same environmental conditions. The total no. of case were 60 patients with similar number of control cases with same age range selected randomly. There was significantly increase in level of epinephrine in all patients. with normal values of epinephrine in all control group. There was statistical differences in Epinephrine level among cases and control group ,The mean + standard deviation of epinephrine level among cases were 49.367 ng /dl + 31.93 , and among control 167.78 ng/dl + 16.53 respectively which is a significant differences. There was a significant relationship in epinephrine level before and after dialysis(epinephrine level decrease significantly after dialysis). Mean +SD for patients before and after dialysis 167+31.92 ,132+25.80 respectively. There was a significant relationship between creatinine level and epinephrine level before dialysis. There was significantly increasing in level of nor epinephrine in all patients, with normal values of nor epinephrine in all control group (both gender male and female). The mean + standard deviation of nor epinephrine level among cases were 696.08 pg /dl + 33.42 , and among control 313.83 pg/dl + 149.62, which is a significant differences While there was a significant relationship between creatinine level and norepinephrine level before dialysis. There was a significant relationship in nor epinephrine level before and after dialysis(nor epinephrine level decrease significantly after dialysis). Mean +SD for patients before and after dialysis 690+33.42, 646+38.56 respectively. It is concluded that there was a significant relationship in epinephrine and nor epinephrine level before and after dialysis and there was a significant relationship between epinephrine, nor epinephrine and creatinine before dialysis.

## **Introduction**

Renal failure can be divided into two categories: acute kidney injury or chronic kidney disease. The type of renal failure is determined by the trend in the serum creatinine. Other factors which may help differentiate acute kidney injury from chronic kidney disease include anemia and the kidney size on ultrasound. Chronic kidney disease generally leads to anemia and small kidney size(1) .

In medicine, dialysis is a process for removing waste and excess water from the blood, and is used primarily to provide an artificial replacement for lost kidney function in people with renal failure. There are three primary and two secondary types of dialysis: hemodialysis (primary), peritoneal dialysis (primary), hemofiltration (primary), hemodiafiltration (secondary), and intestinal dialysis (secondary) (2).

Epinephrine (also known as adrenaline) is a hormone and a neurotransmitter. It increases heart rate, constricts blood vessels, dilates air passages and participates in the fight-or-flight response of the sympathetic nervous system. Chemically, epinephrine is a catecholamine, a monoamine produced only by the adrenal glands from the amino acids phenylalanine and tyrosine (3).

Norepinephrine (INN) (abbreviated norepi or NE) is the US name for nor adrenaline (BAN) (abbreviated NA, NAd, or norad), a catecholamine with multiple roles including as a hormone and a neurotransmitter(4) Areas of the body that produce or are affected by nor epinephrine are described as noradrenergic. The terms nor adrenaline (from the Latin) and nor epinephrine (derived from Greek) are interchangeable, with nor adrenaline being the common name in most parts of the world. (5)

At the present time , one of the main areas of research in renal disease concern with The effect of hemodialysis on plasma nor epinephrine (NE), epinephrine, and dopamine (6).

### **Aim of the study:**

The present study is aimed to evaluate the early change epinephrine and nor epinephrine levels as markers in end stage renal failure.

## **Patients, materials and methods**

A case control study conducted on 60 end stage renal failure patient of both sexes with age range from 1 to 30 years (mean 17.9 ), which carried out during the period from April 2012 to August 2012 in Tikrit Teaching Hospital in renal hemodialysis unit in Tikrit city.

Renal dialysis unit in Tikrit Teaching Hospital is specialized center for treatment ,follow up and research of patients with end stage renal failure. It provides care and treatment for patients with renal failure daily, the patients visit the renal dialysis unit regularly.

### **Group one:-**

Sixty patient with end stage renal failure before dialysis with age range between 1-30 years of both sexes.

### **Group Two:-**

Sixty child and adults were used as controls, these groups consist of apparently healthy individuals with similar age range as above of both sexes and were selected randomly from Apparently healthy

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individuals who were attending for checking and proved to be not patient with end stage renal failure after testing their blood urea and serum creatinine .

Blood samples were obtain from all patients before dialysis by antecubital venepuncture, between 8,30 -9 am, about (4 ml).

(2ml)put directly into disposable tube with EDTA to get plasma to test epinephrine and nor epinephrine, left for 15-30 minute at 37 C.

(2ml) put directly into disposable plain tube, left for 15-30 minute at 37 C for clot formation in water bath , then serum was separate by centrifugation at 3000 rpm for 10 minute, and the sera were frozen at -20 C and kept for analysis at weekly patches ,(for blood urea and serum creatine test).

The same investigations were done to the control group with nearly same environmental conditions.

3. All patients after dialysis by antecubital venepuncture, between 8,30 -9 am, about (6 ml)

2 ml put directly into disposable tube with EDTA to get plasma to test epinephrine and nor epinephrine, left for 15-30 minute at 37 C .

### **Results**

The total no. of case were 60 patients, (45) male 74% .(15) female 26%. With age range between 1-30 years (mean age 17.9 years) .with similar number of control cases, (80%) were males with age range from 1 to 30 years (mean 17.6), ( 20%) were females in age range from 1 – 30 years (mean18.1) selected randomly.

Table (1) shows the age distribution of cases, most of the cases were between 25-30 years , 21 cases (35%) while the lowest age were under 5 years age , 1 case only (1.6%)

Regarding the distribution of patient with chronic renal failure according to gender , it was found that the males were the majority of patients (44person) 74%male but females(16 person) 26% .while in regard to residence, the majority of patients included in this study were from urban area65%(39 person)and the rest from rural 35%(21 person) .

All the study cases had increased both blood urea and serum creatinine as compared to control cases who had normal value of both . This mean that all the cases were actually in renal failure while all the control cases were actually with normal renal function.

Table (2) Shows the plasma concentration of epinephrine as a ( ng/ dl) in patients with renal failure compare with controls in regard to sex, there was significantly increase in level of epinephrine in all patients. with normal values of epinephrine in all control group.

Table 3 Shows the statistical differences in Epinephrine level among cases and control group, the mean + standard deviation of epinephrine level among cases were 49.367 ng /dl + 31.93 , and among control 167.78 ng/dl + 16.53 respectively, this is a significant differences)

Table (4) shows Epinephrine level in patients before and after dialysis. There was a significant relationship in epinephrine level before and after dialysis(epinephrine level decrease significantly after dialysis). Mean

+SD for patients before and after dialysis 167+31.92, 132+25.80 respectively.

There were a statistical significant relation between epinephrine and nor epinephrine level and the serum creatinine level.

Figure (1) show the relation between creatinine level and epinephrine level before dialysis ,  $F= 0.001$ . there was a significant relationship between creatinine level and epinephrine level before dialysis

Table (5) Shows the plasma concentration of nor epinephrine as a(pg/dl) in patients with renal failure compare with controls in regard to gender, there was significantly increasing in level of nor epinephrine in all patients. With normal values of nor epinephrine in all control group (both gender male and female).

Table (6) Shows the statistical differences in Nor-Epinephrine level among cases and control group. The mean + standard deviation of nor epinephrine level among cases were 696.08 pg /dl + 33.42 , and among control 313.83 pg/dl + 149.62, there is a significant differences).

Table (7) shows Nor epinephrine level in patients before and after dialysis. There was a significant relationship in nor epinephrine level before and after dialysis(nor epinephrine level decrease significantly after dialysis). Mean +SD for patients before and after dialysis 690+33.42, 646+38.56 respectively.

## **Discussion**

Chronic kidney disease (CKD) can develop slowly and, initially, show few

symptoms. CKD can be the long term consequence of irreversible acute disease or part of a disease progression(1). Epinephrine :-is a catecholamine, a monoamine produced only by the adrenal glands from the amino acids phenylalanine and tyrosine. Nor epinephrine:- is synthesized from dopamine by dopamine  $\beta$ -hydroxylase. It is released from the adrenal medulla into the blood as a hormone, and is also a neurotransmitter .both elevate in end stage renal failure (2).

The present study indicate the majority of patients and control were males. This agreement with Grünfeld et al There study shows that from 2775 patients (1780 males, 995 females) with  $Scr \geq 200$   $\mu\text{mol/l}$  (6).

The majority of patients and controls were from the urban area and this may be attributed to the number of visits for the urban individuals were higher in comparison with the rural area due to the time they spend to reach the hospital. This agreement with Grünfeld *et al* which have epidemiological study in a large French urban area indicates an incidence of 260 patients per million population annually referred to nephrology units for chronic renal failure defined by  $Scr \geq 200$   $\mu\text{mol/l}$  (6).

Most of the study cases was between the age of 25-30 years and the lowest was below 5 years .This is different from other study by Elias AN, Vaziri ND, Maksy M.(7) which shows totally different age distribution of cases. The reason behind this is may be the difference in the sample size and that our renal unit is a hemodialysis unit only and not for peritoneal dialysis and because hemodialysis is a procedure that need arterio-venous shunt as a route for dialysis and as few children undergoes

arterio-venous shunt as a preparation for transplant and most of them need peritoneal dialysis as a rapid procedure for dialysis which is not available renal unit at Tikrit Teaching hospital and all the patients referred to other renal units in other Governorates.

All the study cases have increased both blood urea and serum creatinine while all control cases have normal values. Urea is derived from amino acids and therefore from protein, whether originated from the diet or from tissues the normal kidney can excrete large amount of urea, creatinine is largely derived from endogenous sources by tissue creatine breakdown. Many laboratories prefer to measure plasma creatinine to assess renal function, if the plasma concentration of either urea or creatinine is significantly raised impaired glomerular function is likely (8). All the patients included in this study were actually affected by chronic renal failure, while the controls were healthy subjects regarding renal function. This finding is attributed to that patients with chronic renal failure were with high blood urea and serum creatinine, and this finding is a fact provided by several studies like Grünfeld et al (6). A rise in blood creatinine level is observed only with marked damage to functioning nephrons. Therefore, this test is suitable for detecting early-stage kidney disease (8).

As shown by this study that the patients had a higher plasma level of both epinephrine and nor epinephrine as compared to controls. This agrees with Elias AN, Vaziri ND, Maksy M. (7). Their results showed that the plasma concentrations of epinephrine and nor epinephrine were significantly elevated in patients with end-stage renal disease,

The reason why both epinephrine and norepinephrine increased in chronic renal disease is that these hormones are stress hormones that increase in any stressful condition like patients with chronic renal failure who are in a continuous stressful condition because of the disease itself or its complications like infections. These results showed that the plasma concentrations of epinephrine and nor epinephrine were significantly elevated in patients with end-stage renal disease.

It was also evident that there was a statistically significant relation between epinephrine level and creatinine level, this is in line with Garg AX, Papaioannou A, Ferko N, Campbell G, Clarke JA, Ray JG study (9) which shows nearly similar results. The reason why is that as mentioned above epinephrine is a stress hormone that increases with increasing stress as increasing severity of renal failure evident by increase in creatinine level. These findings are important in assessing severity of disease at presentation and in the follow up of the index case after treatment.

There was a significant relationship in epinephrine level before and after dialysis (epinephrine level decreased significantly after dialysis). Mean  $\pm$ SD for patients before and after dialysis 167 $\pm$ 31.92, 132 $\pm$ 25.80 respectively which means that the patients with renal failure had some benefit from dialysis. This agrees with Elias AN, Vaziri ND, Maksy M. (7) study which shows that stress hormone decreased in patients with chronic renal failure after treatment. As it was mentioned above epinephrine and norepinephrine as stress hormones decreased as the stressful condition improved and in case of patients

with chronic renal failure specially after dialysis.

**Conclusion**

It is concluded that there was a significant relationship in epinephrine and nor epinephrine level before and after dialysis and there was a significant relationship between epinephrine, nor epinephrine and creatinine before dialysis.

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**Table (1) Age distribution of study cases in years.**

Age distribution	No	%
1-5	1	1.6
5-10	4	6.6
10-15	5	8.3
15-20	9	15
20-25	20	33.3
25-30	21	35
total	60	100

**Table 2** Epinephrine level according to gender

Gender	Case group		Control group	
	Normal values	High values	Normal values	High values
	No(%)	No(%)	No(%)	No(%)
Male	0(%)	50(83.33)	53(88.33)	0(%)
Female	0(%)	10(16.7)	7(11.7)	0(%)
Total	0(%)	60(100)	60(100)	0(%)

**P value =0.432(not significant) , df=1**

**Table 3** The differences in Epinephrine mean among case group and control group

case definition	No.	Mean + SD
Case group	60	167.78+31.93
Control group	60	49.367+16.53
P value(df)	<0.001* (118)	

**\*significant**

**Table 4** Epinephrine level in patients before and after dialysis

case definition	No.	Mean + SD
Case group before dialysis	60	167+31.92
Case group after dialysis	60	132+25.80
P value(df)	<0.001* (59)	

**\*significant**

**Table 5** Nor epinephrine level according to gender

Gender	Case group				Control group			
	Normal values		High values		Normal values		High values	
	No.	%	No.	%	No.	%	No.	%
Male	53	88.33	0	0%	50	83.33	0	0%
Female	7	11.7	0	0%	10	16.7	0	0%
Total	60	100	0	0%	60	100	0	0%

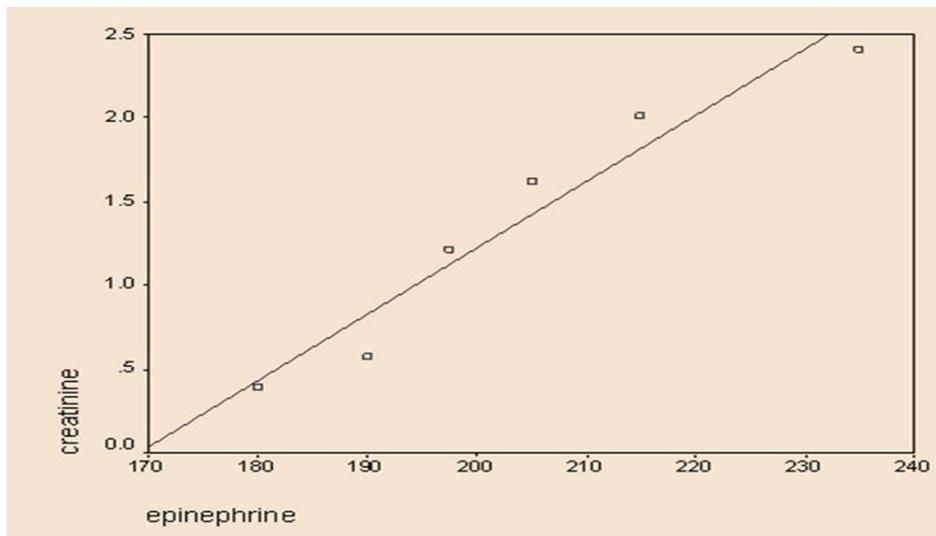
**P value =0.432(not significant) , df=1**

**Table 6** The differences in Nor-Epinephrine mean among case and control group.

case definition	No.	Mean + SD
Case group	60	696.08+33.42
Control group	60	313.83+149.62
P value(df)	<0.001* (118)	

**Table 7** Nor epinephrine level in patients before and after dialysis

case definition	No.	Mean + SD
Case group before dialysis	60	690+33.42
Case group after dialysis	60	646+38.56
P value (df)	<0.001* (59)	



**Fig (1)** show the relation between creatinine level and epinephrine level. F= 0.001 (significant relation).