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Evaluation of TNF-α and TNF-R1 immunomarkers in Renal Failure Patients in Karbala province

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ABSTRACT

Renal failure is characterized by height level of pro-inflammatory cytokines, mainly Tumor necrosis factor-alpha (TNF-α) and its receptor TNF-R1**.** The aim was to investigate the association of TNF-α and TNF-R1 levels in Renal Failure.This study was carried out from February 2022 to March 2023 in the labs of Thi-Qar University's Col1ege of Education for Pure Sciences. In partnership with Al-Hussein Teaching Hospital, Nasiriyah General Hospital, and Thi-Qar Center for Nephrology and Dialysis in Thi-Qar Province .The study comprised (100) patients for both sex : (40 patients with diabetes mellitus), (40 patients without diabetes mellitus) whose serum urea level and serum creatinine level were examined, and (40 healthy).The level of biochemical indicators were measured, which included urea, creatinine, albumin and total protein where the study discovered a considerable rise in urea and creatinine levels compared to healthy subjects and standard rates, and this increase is related 'with a decrease GFR', while there is decrease in rate of albumin and total protein. The statistical analysis' findings revealed a considerable difference ($p < 0.05$) in patients with RF in concentration of the TNF-α and TNF-R1, where they were examined for 80 samples of RF patients, and 40 healthy samples in the control group. The number of RF patients in Thi-Qar province showed a marked increase in the yearly rate of hemodialysis. A third of all patients had a considerable prevalence of RF linked to hypertension. The study concluded that there was a significant effect of TNF-α is associated with markers of kidney disease severity and distant organ dysfunction among patients with RF. In addition, this study found correlation between effects of TNF- α on end-stage renal disease. Extensive studies are needed to confirm these relationships.

***Keywords*:** TNF-α, TNF-R1, Renal Failure

1. INTRODUCTION

A change in kidney structure and function that causes a persistent and increasing leakage of renal function is known as renal failure [1]. Along with urinary tract infections, autoimmune diseases, and other conditions, Diabetes and Hypertension are the most' typical causes of RF [2]. Components of

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serum or urine can be used as diagnostic indicators for renal function tests. Urine biomarkers can be employed for early diagnosis, the identification of mechanism problems, and the severity of dysfunction because they can identify early renal impairment [3].

One significant pro-inflammatory cytokine and crucial component of inflammatory tissue injury is tumor necrosis factor-alpha (TNF-α). Additionally, it performs crucial immunological regulatory tasks. The majority of researchers noted a function of TNF in the etiology of both acute and chronic renal illness. TNF- is the first pro-inflammatory mediator to be released by dendritic cells (DCs) in the renal interstitium following renal injury [4]. Immune cells that infiltrate, primarily macrophages, have been shown to promote the production of tumor necrosis factor in the kidney [5]. TNF-α may change the activity and expression of transporters, which can change the nephron's transport and renal hemodynamics. Organ damage results from the stimulation of immune cell infiltration and cell death [6]. TNF- α is elevated in RF, which is characterized by hypertension, renal injury, and a decline in renal function [7].

TNF-alpha effects are mediated by TNF'-R1, also known as p55, and TNF'-R2, as well as known as p75. Thus, TNF-signaling in the kidney has two different effects. Tumor necrosis factor receptor 1 affects the kidney's defense mechanisms by reducing hyperfiltration while promoting natriuresis, which controls blood pressure. By triggering pro-inflammatory pathways, TNFR2 increases renal tissue damage [8]. Only TNF-R1 is found in the smooth' muscle cells of the renal vasculature, while both (TNFR1 & TNFR2) are expressed in the collecting ducts, proximal tubules, and endothelial cells of the renal vasculature [9]. The kidney's proximal tubule, collecting duct, vascular endothelium, and vascular smooth muscle all contain 'TNF-R1. TNFR1 activity primarily affects the hemodynamic and excretory functions of the kidneys. increases natriuresis and dieresis through TNFR1-mediated activation, decreases GFR, and renal blood flow, the development of renal function has recently been linked to serum TNFR1 level [10] [11]. Additionally, the Josllin Kidney study's findings indicated that elevated 'levels of circulating TNFR1are very good indicator of the progression of diabetic nephropathy into stage 3 or end-stage renal disease [12]. These biomarkers may be highly helpful for RF prognosis and early identification.

2. METHODS AND MATERIALS

2.1. Blood Specimens Collection

This study was carried out from February 2022 to March 2023 in the labs of Thi-Qar University's College of Education for pure sciences in partnership with Al-hussein Teaching hospital, Nasiriyah General Hospital and Thi-Qar Center for Nephrology and Dialysis in Thi-Qar Province, The study comprised (100) participants, for both sex: (40 patients without diabetes mellitus), (40 patients with diabetes mellitus) whose serum urea level and serum creatinine level were examined by pathologists and specialists with expertise in these fields, and (40 healthy). 5 milliliters' of venous blood were obtained using a disposabl syring using aseptic technique from 80 patients and 20 controls via venipuncture. Next, three milliliters were placed directly in a sterile gel tube and allowed to coagulate. After 15 minutes of spinning at 4000 rpm to separate the serum, the tube was frozen at -20 C. These sera were utilized to calculate the interleukin concentration (TNF-α & TNF-R1) in 80 RF patients and 40 controls, where TNF-α and TNF-R1 concentrations' were measured using the (ELISA method) for

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the control group and the infected group. Based on their eGFR', which was determined through serum creatinine testing, the patients were classified into three groups. Blood samples and sera were taken from hospitalized RF patients with a range of etiologies (hypertension, diabetics, hypertensive + diabetic interaction, cardiovascular illnesses, and unexplained etiology).

2.2. Biochemical Analysis

2.2.1. Estimation of Urea: The colorimetric diacetyl monoxide and Berthelot reactions were used to determine the amount of urea. The urea is transform to ammonia' in this technique by an enzyme called urease. In the presence of glutamate dehydrogenase GDH, the ammonia produced is coupled with NADH and 2-oxoglutarate to produce LGlutamate and NAD. The decrease in absorption of NADH is proportional to the concentration of urea [13].

2.2.2.Estimation of Creatinine: The Jaffe reaction, a colorimetric process in which creatinine forms (a yellow-orange complex) in alkaline solution and picric acid, was used to determine creatinine. The color complex is defined photometrically. The color intensity determines amount of creatinine in the sample [13].

2.2.3. Estimation of Albumin: Bromocresolgreen (BCG) method using albumin kit (Ref AB 361) from Randox (U.K). The measurmentof serum albumin is on its quantitative binding to the indicator 3,3,5,5 – tetra bromo-m-cresol sulphonphthalein (bromocresolgreen BCG) without deproteinization. The albumin –BCG complex absorbs maximally at630 nm [14]. •Take 10µL of serum into 2ml of BCG in a test tube marked "T."

•Take 10µL of standard protein solution into 2ml of BCG in a test tube marked "S."

•Take 10µL of distilled water into2ml of BCG test tube marked" B".

Calculation:- Plasma Albumin (g /100ml) = A/ S x Standard concentration (5gm/L)

2.2.4. Estimation of Total protein: The total protein concentration is calculated according to the following equation

Total protein concentration = O.D sample / O.D standard × n

N=7 g/dI

2.3. Immunity Assay

This assay employs to the quantitative sandwich enzyme immunoassay technique. Antibody specific for TNF-α, TNFR has been precoated onto a micro plate. Standards and samples are put into the wells and any TNF-α, TNF-R1 present is bound to the immobilized antibody. After removing any unbound substances, biotin-conjugated antibody specific for TNF-α, TNF-R1 was added to the wells. After washing avidin conjugated Horseradish Peroxidase (HRP) was added to the wells. Following a wash to remove any unbound avidin-enzyme reagent, TMB a substrate solution was added to the wells and color developed in proportion to the amount of TNF-α, TNF-R1 bound in the initial step. reaction is

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terminated by the addition of a sulphuric acid solution and the color change is measured spectrophotometrically at a wavelength of 450 nm.

3. STATICTICAL ANALYSIS

Data analysis was done statistically, and the results were presented as mean SD. Using the computerized Minitab tool, T-test comparisons between each group of RF sufferers and the age-matched healthy controls were carried out. With the computerized Minitab 14 application, comparisons between the three age groups of RF patients were made using analysis of variance (Chi-square, Odds Ratio). The smallest threshold of significance was set at P 0.01. Statistical Package for Social Sciences (SPSS) was used for all statistical analysis (version -23).

4. RESULTS

4.1. Demographic characteristics

Table 1: Show the frequency distribution of renal failure patients with diabetic mellitus ,renal failure patients without diabetic mellitus and control subjects according to sex and residency, the frequency distribution of study groups by sex and residence did not significantly differ (P = 0.113), (P= 0.149) respectively ,as in the illustrated figure (1).'

Table 1: The distribution of' study groups by Sex & Residency.

Characteristic	**Patients with D.M n= 40**	**Patients without D.M n= 40**	**Control n=40**	***Mean***	***P. value***
Sex					
Male, *n* (%)	34 (85.00%)	26 (65.00 %)	24 (70.00 %)	74 (74.00 %)	0.113 (N.S)
Female, *n* (%)	6 (15.00 %)	14 (35.00%)	16 (30.00%)	26 (26.00%)	
(N.S)- no significant Df =1 P.value=0.113					
Characteristic	**Patients with D.M n= 40**	**Patients without D.M n= 40**	**Control n=40**	***Mean***	***P. value***
Residency					
Urban, n (%)	32 (80.00 %)	24 (60.00%)	24 (60.00%)	70 (70.00 %)	0.149 N.S
Rural, n (%)	8 (20.00%)	16 (40.00 %)	16 (40.00 %)	30 (30.00%)	
(N.S)- no significant Df =1 P.value=0.149					

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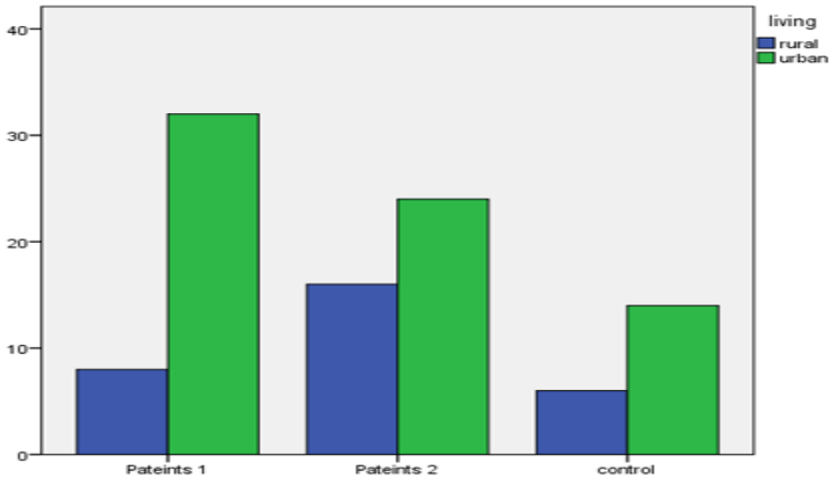

Figure 1: distribution of study groups according to Residency

The results in **table 2** indicated a significants increase (P = 0.008), in the percentage of non-smokers patients ,also the findings of our current research also explained that there is no significant difference according to 'the family history (P= 0.106) , and the outcomes indicated a significant increase according to hypertension where (P= 0.001) ,as in the illustrated figure (2,3,4).

Table 2: Distribution of study groups according to Smoking, Family history and hypertension.

Characteristic	**Patients with D.M n= 40**	**Patients without D.M n= 40**	**Control n=40**	***Mean***	***P. value***
Smoking					
Yes, *n* (%)	0 (0.00%)	2 (05.00 %)	4 (20.00 %)	6 (6.00 %)	0.008 *
No, *n* (%)	40 (100 %)	38 (95.00%)	36 (80.00%)	94 (94.00%)	
Df =1		P.value=0.008*			
Family History					
Yes, *n* (%)	8 (20.00%)	6 (15.00 %)	0 (0.00 %)	14 (14.00 %)	0.106
No, *n* (%)	32(80.00%)	34 (85.00%)	40 (100 %)	86 (86.00%)	(N.S)
(N.S)- no significant		Df =1		P.value=0.106	
Hypertension					
Yes, n (%)	38 (95.00%)	24 (60.00 %)	4 (20.00%)	66 (66.00 %)	0.001

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No, *n* (%)	2 (05.00 %)	16 (40.00%)	36 (80.00%)	34 (34.00%)	
		Df =1	P.value=0.001		

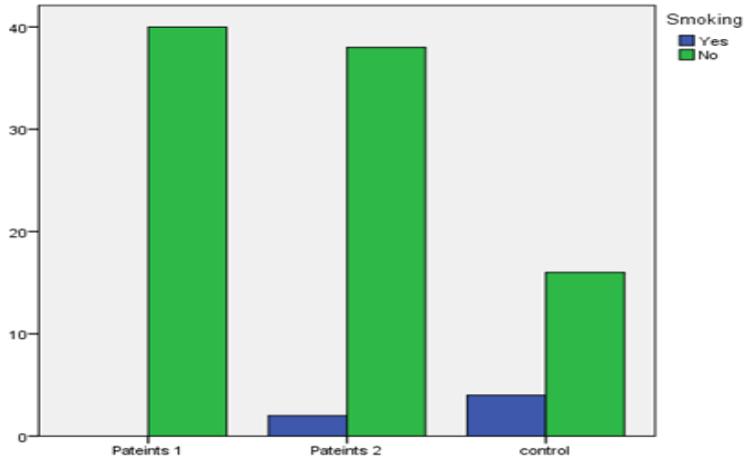

Figure 2: distribution of study groups according to Smoking.

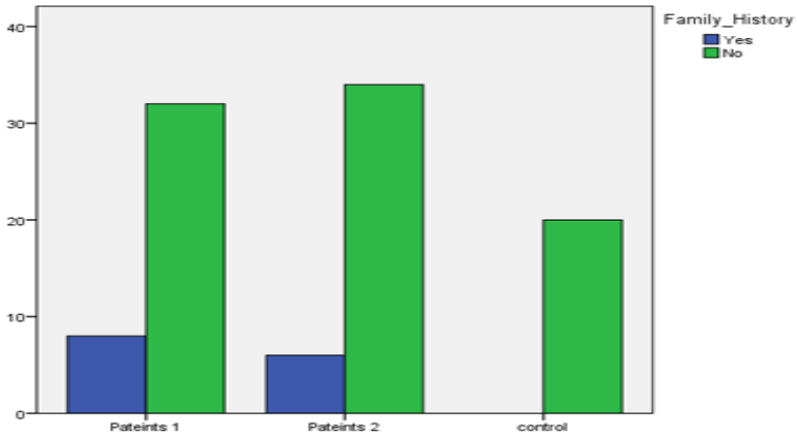

Figure 3: distribution of study groups according to Family history.

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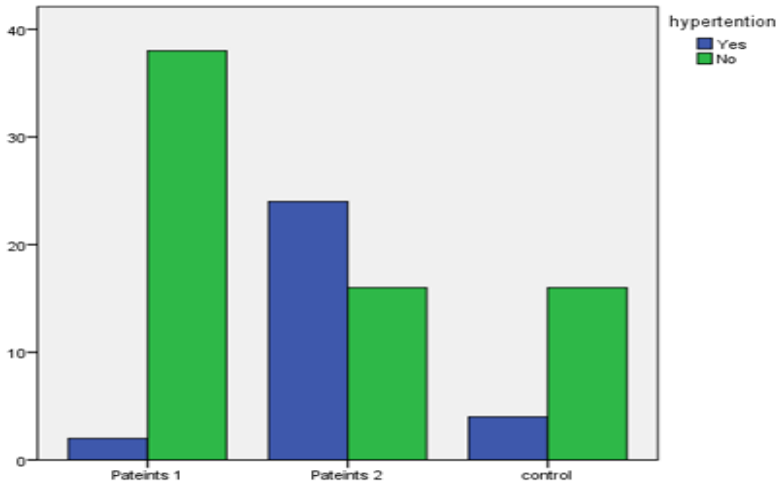

Figure 4: distribution of study groups according to Hypertension.

The current results in table (3,4,5,6), be seen a significant increase of both urea, creatinine, albumin and total protein levels comparing with control group.

Table 3: Distribution of study groups according to Urea.

Urea				***P. Value***
	Groups	**Mean ± SD**	**N**	
Male	Diabetes	111.088 ± 19.8179	34	0.027 *
	Non Diabetes	141.231 ± 25.0955	26	
	control	16.857 ± 2.0327	24	
	Total	103.851 ± 48.6558	84	
Female	Diabetes	96.667 ± 27.3252	6	
	Non Diabetes	144.357 ± 12.6467	14	
	control	15.000 ± .0000	16	
	Total	103.500 ± 55.3015	36	
Total	Diabetes	108.925 ± 21.3366	40	0.001 **
	Non Diabetes	142.325 ± 21.4313	40	
	control	16.300 ± 1.8946	40	
	Total	103.760 ± 50.1793	120	

Table 4: Distribution of study groups according to Creatinine.

Creatinine				***P. Value***
	Groups	**Mean ± SD**	**N**	
Male	Diabetes	5.553 ± 1.2432	34	
	Non Diabetes	6.108 ± 2.1520	26	

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	control	0.900 ± 0.2542	24	
	Total	4.868 ± 2.4661	84	
Female	Diabetes	4.667 ± 1.3663	6	0.674 N,S
	Non Diabetes	8.386 ± 2.5854	14	
	control	1.100 ± 0.3225	16	
	Total	5.846 ± 3.6362	36	
Total	Diabetes	5.420 ± 1.2845	40	
	Non Diabetes	6.905 ± 2.5313	40	0.01 **
	control	0.960 ± 0.2836	40	
	Total	5.122 ± 2.8301	120	

Table 5: Distribution of study groups according to Albumin.

Albumin				
Sex	**Groups**	**Mean ± SD**	**N**	***P. Value***
Male	Diabetes	39.824±3.7535	34	
	Non Diabetes	37.692±5.1596	26	
	control	42.071±1.1269	24	
	Total	32.311±14.3266	84	
Female	Diabetes	39.000±2.3664	6	0.63 N.S
	Non Diabetes	39.429±6.1982	14	
	control	43.367±.8116	16	
	Total	31.008±16.1132	36	
Total	Diabetes	39.700±3.5677	40	
	Non Diabetes	38.300±5.5294	40	0.001 **
	control	43.860±1.0733	40	
	Total	31.972±14.7391	120	

Table 6: Distribution of study groups according to Total protein.

Protein				
Sex	**Groups**	**Mean ± SD**	**N**	***P. Value***
Male	Diabetes	60.000 ±5.1874	34	
	Non Diabetes	63.038 ±7.0738	26	
	control	70.943 ±.8803	24	
	Total	61.219 ±21.7779	84	
Female	Diabetes	62.667 ±3.6148	6	0.199 N.S
	Non Diabetes	65.357 ±11.2017	14	

	control	78.067 ±1.5552	16	
	Total	63.515 ±25.6623	36	
Total	Diabetes	60.400 ±5.0373	40	0.001 **
	Non Diabetes	63.850 ±8.6693	40	
	control	70.980 ±1.0817	40	
	Total	61.296 ±22.7165	120	

The current results in **table 7**, showed a significant increase of TNF-α.

Table 7: Distribution of study groups according to TNF-α.

TNF-α pg/ml				***P.Value***
Sex	**Groups**	**Mean ± SD**	**N**	
male	Diabetes	0.83153 ±1.896893	34	0.708 N.S
	Non Diabetes	0.65581±0.897528	26	
	control	0.24386 ±0.471078	24	
	Total	0.65861 ±1.410283	84	
female	Diabetes	1.64233 ±3.157125	6	
	Non Diabetes	0.56529 ±0.653088	14	
	control	0.01067 ±0.007711	16	
	Total	0.68585±1.597626	36	
Total	Diabetes	0.95315 ±2.099638	40	0.01 *
	Non Diabetes	0.62412 ±0.812692	40	
	control	0.17390 ±0.404811	40	
	Total	0.66569 ±1.453015	120	

The current study statistical evolution in the mean TNFR1 levels in RF patients.

Table 8: Distribution of study groups according to TNF-R1.

TNF-R1 pg/ml				
Sex	**Groups**	**Mean ±Std. Deviation**	**N**	***P. Value***
male	Diabetes	16.40974 ±4.061753	34	0.06 N.S
	Non Diabetes	12.13250 ±5.295295	26	
	control	9.95071 ±3.299378	24	
	Total	13.68495 ±5.098034	84	
female	Diabetes	17.97283 ±8.757281	6	
	Non Diabetes	15.10643 ±6.598849	14	

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	control	11.15667 ±1.704290	16	
	Total	14.85642 ±6.649306	36	
Total	Diabetes	16.64420 ±4.910322	40	0.001 *
	Non Diabetes	13.17337 ±5.878184	40	
	control	10.31250 ±2.921317	40	
	Total	13.98953 ±5.531363	120	

5. DISCUSSION

Renal failure (RF) disease has been more common over the past three decades, although the fundamental causes of this ailment are still poorly understood. Where renal failure is a medical condition where the kidneys are working at less than 15% of normal levels and can no longer effectively filter waste materials from the blood [15]. The findings of current study demonstrated that there is no significant difference between the (2groups) of patients and healthy people according to sex. Despite the samples being randomly chosen, the result showed that the RF patients can affect both sexes and is unrelated to the nature of sex, also this study showed that there is no significant difference between the two groups of patients and healthy people according to residency [16].

The results in table (2) indicated a significant increase (P= 0.008) in the percentage of non-smokers patients , Finding the risk factors for the advancement of renal failure is the most important crucial challenges of experimental and clinical nephrology. A smoking is a significant renal risk factor, that despite mounting data, hasn't received enough attention. The negative effects of smoking on the kidneys were initially identified by diabetologists; where smoking raises the risk of developing nephropathy' in both (type 1 & 2) diabetes and (ii) nearly doubles the rate at which end-stage renal failure progresses. It was not known until recently if smoking increased the probability that people with primary renal illness may proceed to end-stage renal failure. A retrospective multicenter European case-control study has revealed that smoking independent risk factor for end-stage renal failure. Smoking increases the chance of developing end-stage renal failure in patients with both inflammatory and non-inflammatory renal diseases, such as polycystic kidney disease and IgA glomerulonephritis.according to a retrospective multicenter European case-control research. The cause of the kidney impairment brought on by smoking is mainly unknown. One key factor in the development of renal injury while smoking appears to be the occasional rise in blood pressure. Both diabetologists and nephrologists are quite interested in smoking as a renal risk factor, but sadly, patient management has not changed much as a result of this information to date [17]. The results of our current study also, showed that there is no significant' difference according to the family history, as kidney failure could be caused by other causes that may be immunological or genetic, or as a result of taking certain medications without consulting the specialist doctor.

The results in table (2) indicated a significant increase according to hypertension, where (P= 0.001) .There are still certain risk factors that can turn RF into ESRD. However, in some low-income nations as well as middle- and high-income countries, DM and HTN are 'the primary causes of RF [18]. The current investigation demonstrated the incidence of related disorders in RF patients, including HTN, DM, and diseases with unclear causes.95 % of the 80 total patients have connections between diabetes and hypertension. Since 60% of patients had hypertension, this disease had the second-highest

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prevalence rate among its linked conditions. The most frequent interactions between hypertensive and diabetic patients were those with hypertension, diabetes, and an unclear etiology. Most people with diabetic kidney disease (DKD) have hypertension, which affects them twice as frequently as the general population [19].

The risk of developing and progressing chronic kidney disease is considerably increased by having both diabetes mellitus and hypertension, especially when these conditions are not effectively treated. However, the significance and interactions of these factors are still unknown [20]. Some pathological mechanisms, such as activation of the renin-angiotensin-aldosterone system, mechanical stretch, endoplasmic reticulum (ER) stress, oxidative stress, apoptosis, and mitochondrial dysfunction, were proposed to contribute to diabetichypertensive nephropathy. Numerous studies suggest that the rapid evolution of diabetic nephropathy may need hypertension. Chronic mechanical stresses associated with increases in hypertension may interact with hyperglycemia, damaging the kidneys. More than 50% of RF patients have hypertension and blood pressure above 140/90 mm Hg, which is one of the key contributing factors to RF advancement and an increase in RF risk [21]. Uncertainty surrounds the precise processes of kidney injury in people with hypertension. Two complementary pathologic processes that eventually lead to renal scarring and fibrosis have been proposed.One starts with changes to the macro and micro vasculature of the system and the kidneys, which create a decrease in renal autoregulation, an increase in intraglomerular capillary pressure, and the harm brought on by hyperfiltration as a result. Transglomerular protein loss caused by hyperfiltration encourages downstream tubular epithelial and mesangial cells to release growth factors and cytokines.

The current results in tables (3,4), be seen a significant increase of both urea and creatinine levels comparing with control group, the results were in line with other research [22] [23], which demonstrated that pre-hemodialysis patients had higher serum levels of urea and creatinine than healthy volunteers for both sexes. Urea is one of the by products of protein 'metabolism, produced in the liver and eliminated through urine, which accounts for the increase in urea levels. When a patient has kidney failure, urea builds up in their blood and causes uremia [24]. It is thought that creatinine, an amino acid molecule produced from creatine, has ruminant metabolism. It is continuously released into the plasma, Freely filtered by the glomerulus, and not reabsorbed or metabolized by the kidney, resulting in normal excretion in the urine [25]. The abnormality in renal filtration rate associated with RF may cause a rise in creatinine levels that is inversely related to the glomerular filtration rate [25]. Relatively reports, the body converts 2% of its creatine into creatinine each day, causing the body to produce a pretty constant amount of creatinine every day [25]. Additionally, this study discovered that, as compared to female patients, male patients had higher urea and creatinine levels. These findings are consistent with those of [26] [27]. However, an individual's dietary health, muscle mass, age, and sex have a substantial impact on these levels [23]. Though the condition is more severe' in males, who also have a highest frequency of ESRD, C K D tend to be more common in women (dialysis). With the exception of post-menopausal women and patients with diabetes, the majority of the evidence points to a higher rate of CKD progression and mortality risk in men as compared to women.

As for albumin, the results of the current study were consistent with the results of the study conducted by the researchers [28] which states that albumin is lower in patients with renal failure compared to healthy subjects. This decrease in albumin levels can be attributed to the following reasons, changes in the structure of the basement membrane of the glomeruli that result in leakage of albumin and some proteins of low molecular weight, as the excretion of protein with urine is a sign of the development of renal disease, and restriction in taking protein (diet) and protein malnutrition may be attributed to such

a decrease in albumin in the patients' serum [29]. [30] indicated that low albumin is one of the severe clinical signs of hepatic cell disease caused by impaired albumin synthesis. Also, this decrease may be attributed to increased albumin loss as a result of glomerulonephritis. [28] pointed out that the reason for the decrease in albumin in the blood serum is attributed to the damaged tissue of the kidneys or as a result of fluid retention. Or albumin may decrease as a result of a decrease in the concentration of calcium in the blood, as almost 50% of blood plasma calcium is combined with albumin [31]. The reason for the decrease in albumin is also due to its consumption by the body as an antioxidant [32], as [33] indicated that albumin is one of the blood plasma proteins containing the thiol group (-SH) and as an antioxidant it protects the body from the effects of free radicals and active oxygen species (ROS) and therefore it inhibits the process of lipid peroxidation that leads to damage to cellular components, and therefore a decrease its level in the serum of patients with failure may indicate an increase in the state of oxidative stress due to free radicals [34] [35]. Also, renal function deterioration is substantially and independently correlated with lower blood albumin levels, regardless of clinical risk factors, urine albumin, or assessed inflammatory markers, the results of the current study agree with the results of the study conducted by the researchers [36].

As for the total protein, the results of the current study were consistent with the results of the study conducted by the researchers [37] where it was found in the current study a decrease in the concentration of total protein in the serum of patients with renal failure compared to healthy subjects.The high concentration of total protein in the blood serum of patients is logical for several reasons, the most important of which is the failure of the kidneys in the process of filtering proteins and their crossing the level of the renal threshold, and thus their descent with diuresis, which leads to a rise in the concentration of total protein in the blood serum. In addition to the association of many types of urea toxins with total protein, and thus works to raise the levels of total protein concentration in the blood serum of patients with renal failure [38] [39].

The current results in table (7), showed a significant increase of TNF-alpha. Relatively studies, renal tubular epithelial cells are one type of cell that release TNF. It has a significant role in glomerular fibrosis and inflammation by promoting the secretion of interleukin-1β and TGF-1 [40][41]. Patients with various renal diseases have been found to have higher-than-normal TNF- levels. In addition, infliximab's TNF suppression reduces the course of CKD in a variety of animal models [42]. TNF receptor 1 (TNFR1) mediates the effects of TNF [43]. According to [41], a number of renal disorders result in an increase in the expression of this receptor and its shedding from the cell membrane. By neutralizing free TNF, soluble TNFR may reduce inflammation and so represent a possible antifibrotic treatment in CKD [41].

The current study statistical evolution in the mean TNFR1 levels in RF patients, according to a study by [44], patients with renal failure had significantly higher levels of TNFR1 in their patient sera than the control group. Depending on [45], there is a substantial correlation between TNFR1 concentrations and the likelihood of early renal deterioration. According to sex, the study showed an increase in TNFR1 mean serum concentration in RF patients compared with the control group. This finding is consistent with those of [46], [47], [48], who showed evaluated circulating levels of TNFR1 for both male and female patients. Additionally, TNFR1 inducer of promotes tubular cell injury, renal inflammation, and renal fibrosis in a number of ways, including by promoting fibroblast proliferation or their differentiation into (ECM-producing myofibroblasts), by encouraging the formation of Pro-inflammatory mediators by Tubular cells, by down-regulating the antifibrotic molecule Klotho in tubular cells, and through actions on other cell types such as pericytes and podocytes [49][50].

6. CONCLUSION

In the province of Thi-Qar, TNF-alpha and TNF-R1 were discovered to be connected to RF susceptibility or severity. Also there was high proportion of unknown causes due to late diagnosis, late referral, inappropriate care on early stage 1, 2 and 3 CKD and insufficient imaging study diagnosis. But hypertension and diabetic mellitus are the important risk factors that cause and advances renal failure disease. where the significant prevalence of RF associated with hypertension was about third of total patients.

7. AUTHORS' CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data , or analysis and interpretation of data , took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

8. FUNDING

There is no funding to report.

9. CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

10. ETHICAL APPROVALS

This study does involve experiments on human subjects with the consent of the patient.

11. DATA AVAILABILITY

All data generated and analyzed are included within this research article and the sequences are available online in the NCBI database.

12. PUBLISHER'S NOTE

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REFERENCES

[1] Afkarin, Maryam, et al. Clinical manifestations of kidney disease among US adults with diabetes, 1988-2014. Jama, 2016, 316.6: 602-610.

[2] Ghonemy, Tarek A., et al. Epidemiology and risk factors of chronic kidney disease in the El-Sharkia Governorate, Egypt. Saudi Journal of Kidney Diseases and Transplantation, 2016, 27.1: 111.

[3] Humphreys, Benjamin D.; BONVENTRE, Joseph V. Mesenchymal stem cells in acute kidney injury. Annu. Rev. Med., 2008, 59: 311-325.

[4] Singbartl, Kai; FORMECK, Cassandra L.; KELLUM, John A. Kidney-immune system crosstalk in AKI. In: Seminars in nephrology. WB Saunders, 2019. p. 96-106.

[5] Parameswaran, Narayanan; PATIAL, Sonika. Tumor necrosis factor-α signaling in macrophages. Critical Reviews™ in Eukaryotic Gene Expression, 2010, 20.2.

[6] Ramseyer, Vanesa D.; GARVIN, Jeffrey L. Tumor necrosis factor-α: regulation of renal function and blood pressure. American Journal of Physiology-Renal Physiology, 2013, 304.10: F1231-F1242.

[7] Therrien, Frédérick J., et al. Neutralization of tumor necrosis factor-alpha reduces renal fibrosis and hypertension in rats with renal failure. American journal of nephrology, 2012, 36.2: 151-161.

[8] Mehaffey, Eamonn P., et al. Intrarenal angiotensinogen production induced by chronic angiotensin II and high salt intake is augmented in tumor necrosis factor-alpha receptor type 1 knockout mice. The FASEB Journal, 2016, 30: 1216.13-1216.13.

[9] Castillo, Alexander, et al. Tumor necrosis factor-α receptor type 1, not type 2, mediates its acute responses in the kidney. American Journal of Physiology-Renal Physiology, 2012, 302.12: F1650-F1657.

[10] Majid, Dewan SA. Tumor necrosis factor-α and kidney function: experimental findings in mice. In: Advances in TNF Family Research: Proceedings of the 12th International TNF Conference, 2009. New York, NY: Springer New York, 2010. p. 471-480.

[11] Xun, Chunhua; ZHAO, Yong. Potential role of soluble TNF-α receptors in diagnosis of patients with chronic kidney disease. Annals of Clinical & Laboratory Science, 2017, 47.3: 310-314.

[12] Niewczas, Monika A., et al. Circulating TNF receptors 1 and 2 predict ESRD in type 2 diabetes. Journal of the American Society of Nephrology, 2012, 23.3: 507-515.

[13] Amin, Noor, et al. Evaluating urea and creatinine levels in chronic renal failure pre and post dialysis: a prospective study. Journal of cardiovascular disease, 2014, 2.2: 1-4.

[14] Doumas, Basil T.; WATSON, W. Ard; BIGGS, Homer G. Albumin standards and the measurement of serum albumin with bromcresol green. Clinica chimica acta, 1971, 31.1: 87-96.

[15] Obesity, Weight Loss; RANGE, Number Sex Age. Clinical Research Protocol National Institute of Diabetes and Digestive and Kidney Diseases. 2017.

[16] Poon, Richard KS. Chronic kidney disease in the elderly: assessment and management. Australian family physician, 2012, 41.12: 940-944.

[17] Zeier, Martin; RITZ, Eberhard; RONCO, C. (ed.). Nephrology Grand Rounds. Clinical Issues in Nephrology. S. Karger, 1998.

[18] Ahmed, Hussain Gadelkarim, et al. Etiology of chronic kidney disease (ckd) in Saudi Arabia. International Journal of Medical Research & Health Sciences, 2019, 8.5: 177-182.

[19] Patney, Vikram; WHALEY-CONNELL, Adam; BAKRIS, George. Hypertension management in diabetic kidney disease. Diabetes Spectrum, 2015, 28.3: 175-180.

[20] Wang, Xuening; XIAO, Shengxiang; XIA, Yumin. Tumor necrosis factor receptor mediates fibroblast growth factor-inducible 14 signaling. Cellular Physiology and Biochemistry, 2017, 43.2: 579-588.

[21] Puch, Dan; GALLACHER, Peter J.; DHAUN, Neeraj. Management of hypertension in chronic kidney disease. Drugs, 2019, 79: 365-379.

[22] Mosa, Azzam Abdulsattar. The Effect of Some Risk Factors Participating in the Incidence of Chronic Renal Failure. JOURNAL OF THI-QAR SCIENCE, 2011, 3.1.

[23] Aljebory, Abdulhussien MK, et al. Effect of Kidney Dialysis on Some Biochemical Variance. In: Journal of Physics: Conference Series. IOP Publishing, 2019. p. 052019.

[24] Sarhat, Entedhar Rifaat; MURTADHA, Nawal Abdullah. Biochemical changes in chronic renal failure pre and post hemodialysis. Journal of Environmental Science and Engineering A, 2016, 190.

[25] Asif, Abuzar A.; HUSSAIN, Habiba; CHATTERJEE, Tulika. Extraordinary creatinine level: a case report. Cureus, 2020, 12.7.

[26] Caravaca, Francisco, et al. Uraemic symptoms, nutritional status and renal function in pre-dialysis end-stage renal failure patients. Nephrology Dialysis Transplantation, 2001, 16.4: 776-782.

[27] Rajendran, N. Biochemical evaluation of creatinine and urea in patients with renal failure undergoing hemodialysis. Journal of Clinical Pathology and Laboratory Medicine, .,(2017) ,1(2), 1–5.

[28] Rule, Andrew D., et al. A comparison of serum creatinine–based methods for identifying chronic kidney disease in hypertensive individuals and their siblings. American journal of hypertension, 2006, 19.6: 608-614.

[29] Farhan, L. Determanation of Several Biochemical Markers in Sera of Patients with Kidney Diseases. Journal of Al-Nahrain University Science, .,(2013),16(3), 40–45.https://doi.org/10.22401/jnus.16.3.05

[30] Tabrizi, Bahram Amouoghli; KARAROUDI, Meisam Naeimi. Evaluation of Serum Levels of AST, ALT, Total Bilirubin, FBC, Urea, and Creatinine After Administration of 99mTc-MIBI in Mice. American Journal of Clinical Pathology, 2012, 138.suppl_1: A016-A016.

[31] Komatsu, Mizuki, et al. A low serum albumin level predicts cardiovascular events in hemodialysis patients with preserved left ventricular ejection fraction. International Journal of Clinical Medicine, 2015, 6.02: 85-95.

[32] Mohammed, Doaa Jassim; Abd al-Rahman, owner of Juma'a; Money, shame Sami.. A comparative study of the effectiveness of some liver enzymes in chronic renal failure patients with hepatitis (C) and (B). Journal Tikrit Pure Sciences.2013, 54.

[33] Delaney, Anthony P., et al. The role of albumin as a resuscitation fluid for patients with sepsis: a systematic review and meta-analysis. Critical care medicine, 2011, 39.2: 386-391.

[34] Demir, H., et al. Ischaemia-modified albumin elevation after percutaneous coronary intervention reflects albumin concentration rather than ischaemia. Annals of clinical biochemistry, 2009, 46.4: 327-331.

[35] Tristyanto, Agung; SUROTO, Heri. The Clinical Function Comparison of Post Operative Nerve Grafting and Nerve Transfer in Patients with Brachial Plexus Injury. Indian Journal of Forensic Medicine & Toxicology, 2020, 14.2: 2013-2018.

[36] Mimic-Oka, J.; Simic, T.; Pljesa, M.; Stupar, N.; and Turkovic, S. Oxidative Modifcations of Plasma Proteins in Different Stages of Chronic Renal Failure. Med. and Biol, (2001). 8. Pp : 1-5.

[37] Jain, Ram B.; DUCATMAN, Alan. Perfluoroalkyl acids serum concentrations and their relationship to biomarkers of renal failure: Serum and urine albumin, creatinine, and albumin creatinine ratios across the spectrum of glomerular function among US adults. Environmental research, 2019, 174: 143-151.

[38] Lang, Joshua, et al. Association of serum albumin levels with kidney function decline and incident chronic kidney disease in elders. Nephrology Dialysis Transplantation, 2018, 33.6: 986-992.

[39] Molnar, Miklos Z., et al. High platelet count as a link between renal cachexia and cardiovascular mortality in end-stage renal disease patients–. The American journal of clinical nutrition, 2011, 94.3: 945-954.

[40] Lesaffer, Gerrit, et al. Intradialytic removal of protein-bound uraemic toxins: role of solute characteristics and of dialyser membrane. Nephrology Dialysis Transplantation, 2000, 15.1: 50-57.

[41] Pallos, Debora, et al. Salivary markers in patients with chronic renal failure. Archives of oral biology, 2015, 60.12: 1784-1788.

[42] Lee, So-Young; KIM, Sung I.; CHOI, Mary E. Therapeutic targets for treating fibrotic kidney diseases. Translational Research, 2015, 165.4: 512-530.

[43] Idasiak-Piechocka, Ilona, et al. Urinary excretion of soluble tumour necrosis factor receptor 1 as a marker of increased risk of progressive kidney function deterioration in patients with primary chronic glomerulonephritis. Nephrology Dialysis Transplantation, 2010, 25.12: 3948-3956.

[44] Quiroga, Borja, et al. Present and future in the treatment of diabetic kidney disease. Journal of diabetes research, 2015, 2015.

[45] Oh, Sung-Man, et al. Assessing the recovery from prerenal and renal acute kidney injury after treatment with single herbal medicine via activity of the biomarkers HMGB1, NGAL and KIM-1 in kidney proximal tubular cells treated by cisplatin with different doses and exposure times. BMC complementary and alternative medicine, 2017, 17.1: 1-9.

[46] Mezil, Sabreen Ali; ALLAWI, Ali Abdulmajid Dyab; GHUDHAIB, Kadhim K. Determination of TNFR1 Level and its Association with ACR and eGFR in Iraqi Patients with Different Stages of Diabetic Nephropathy. Journal of Global Pharma Technology, 2018, 10.05: 449-454.

[47] NIEWCZAS, Monika A., et al. Circulating TNF receptors 1 and 2 predict ESRD in type 2 diabetes. Journal of the American Society of Nephrology, 2012, 23.3: 507-515.

[48] Kumar, Ajay, et al. Effect of Drug therapy on transforming growth factor-β levels in end stage renal disease patients.

[49] Pavkov, Meda E., et al. Tumor necrosis factor receptors 1 and 2 are associated with early glomerular lesions in type 2 diabetes. Kidney international, 2016, 89.1: 226-234.

[50] Lv, Wenshan, et al. Inflammation and renal fibrosis: recent developments on key signaling molecules as potential therapeutic targets. European journal of pharmacology, 2018, 820: 65-76.