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PENTRAXIN 3 AND ATHEROSCLEROSIS IN CHRONIC KIDNEY DISEASE PATIENTS UNDER HAEMODIALYSIS AND RENAL REPLACEMENT TREATMENT

By

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ABSTRACT

Background: Chronic kidney disease (CKD) is a major widespread public health problem worldwide. Several studies showed the association between biomarkers of systemic inflammation, as C-reactive protein (CRP), Interleukin-6 (IL-6), tumor necrosis factor-alpha and fibrinogen, with lower kidney function pentraxin 3 (PTX3) is elevated in dialysis patients compared to healthy controls and reflects endothelial dysfunction associated with cardiovascular disease (CVD) and mortality risk. Persistent high PTX3 levels are associated with high mortality risk in hemodialysis patients.

Objective: This study was designed to investigate serum level of PTX3 in patients under regular hemodialysis and those who receive renal transplant.

Patients and methods: This was a cross-sectional study involving 90 subjects divided into equal 3 groups: Group (1): 30 healthy subjects (Control) matched for age and sex with patients groups (19 females, 11 males, mean age: 36.9 ± 8.9 years) between January 2017 and November 2019, Group (2): Renal transplant (Rtx) patients (16 females, 14 males; mean age: 40.0 ± 13.3 years), and group (3) 30 patients on hemodialysis (HD) (18 females, 12 males; 46.6 ± 10.7 years) followed at least 6 months in the transplantation and dialysis units of El Maadi Military Hospital and All patients enrolled in the study were randomly assigned. Rtx patients received their grafts and dialysis patients received HD treatments at least 6 months prior to the study. All patients and control were recruited from El Maadi Military Hospital.

Results: Blood pressure, TLC, neutrophils, lymphocytes, creatinine, urea, cholesterol, phosphorus, calcium phosphorus product and CRP were significantly increased in patients groups when compared to control group. PTX3 ranged from 0.50 to 10.20 and there was significant increase in HD group (2.39±1.14) and RT group (5.18±1.62) when compared to control group (1.00±0.35). In addition, there was significant increase in RT when compared to HD group. CIMT ranged from 0.4 to 0.88 and there was significant increase of CIMT in HD (0.85±0.02) and RT group (0.84±0.03) when compared to control group (0.55±0.11); but the difference between HD and RT groups was statistically non-significant. In HD group, PTX3 was proportionally and positively correlated with CIMT, cholesterol and LDL and inversely correlated with TLC. In RT group, there was positive (proportional), significant correlation between PTX2 and each of CIMT, cholesterol, TG, LDL, creatinine clearance and calcium; while there was inverse (negative) correlation between PTX3 and HDL.

Conclusion: The plasma levels of PTX3 may server as suitable biomarkers for cardiovascular disease in hemodialysis and renal transplant patients.

Keywords: Pentraxin 3, Atherosclerosis, Chronic kidney disease, Haemodialysis, Renal Replacement.

INTRODUCTION

Chronic kidney disease (CKD) is a major widespread public health problem worldwide. CKD progresses irreversibly and may lead to end-stage renal disease (ESRD). CKD and ESRD are linked to an increased risk of mortality, cardiovascular complications and comorbidities, and high costs for the treatment of renal failure with dialysis or transplantation *(Feldreich et al., 2019)*.

Many of the traditional cardiovascular risk factors such as age, sex, dyslipidemia, diabetes mellitus and smoking do not appear to adequately explain the high cardiovascular risk in ESRD patients. As a consequence, managing ESRD-related CVD with standard clinical interventions is deemed suboptimal *(Liu et al., 2014)*.

Instead, non-traditional risk factors (such as mineral metabolism abnormalities, uremic toxins, and inflammation) contribute to cardiovascular pathology in ESRD, but little is known about which factors in the vascular milieu of hemodialysis patients are most important *(Liu et al., 2018)*. A persistent mild-to-moderate inflammation is common in CKD patients and enhanced in ESRD patients. Inflammation is able to amplify other common features, as oxidative stress, atherosclerosis, vascular calcification, depression and protein energy wasting, acting as a catalyst of risk factors for ESRD *(Coimbra et al., 2017)*. Several studies showed the association between biomarkers of systemic inflammation, as CRP, IL-6, tumor necrosis factor-alpha and fibrinogen, with lower kidney function *(Lin et al., 2010)*.

Pentraxin 3 (PTX3), is produced by acquired and innate immunity cells in peripheral tissues. It increases rapidly within the primary local of activation, triggering the inflammatory response. Thus, while CRP is produced by hepatocytes, PTX3 is synthesized at the site of inflammation. It increases as renal function declines and predicts CV and overall mortality risk in CKD patients. PTX3 also plays regulatory functions in angiogenesis, atherosclerosis, apoptotic cell clearance and tissue repair *(Witasp et al., 2013)*.

The rapid increase in PTX3 expression in vascular endothelial cells, following an inflammatory stimulus, showed that it could be a useful marker for vascular pathology. Indeed, PTX3 seems to be a powerful marker of inflammation and a good biomarker for development and progression of atherosclerosis *(Coimbra et al., 2017)*.

PTX3 is elevated in dialysis patients compared to healthy controls and reflects endothelial dysfunction associated with CVD and mortality risk *(Sangeetha et al., 2018)*. Also, Plasma PTX3 is considered as an inflammatory marker of endothelial dysfunction, linked to increasing cardiovascular mortality risk *(Norata et al., 2010)*.

PTX3 levels is high in patients with advanced chronic kidney disease and those under regular hemodialysis, but higher in the later group. Patients with cardiovascular disease, in both groups, it had the highest concentrations *(Chmielewski et al., 2015)*. Persistent high PTX3 levels are associated with high

mortality risk in hemodialysis patients *(Sjober et al., 2014)*.

This work was designed to study serum level of PTX3 in patients under regular hemodialysis and in renal transplant recipients. To evaluate the relationship between PTX3 levels and atherosclerotic changes among them.

PATIENTS AND METHODS

This was a cross-sectional study involving 90 subjects divided into equal 3 groups: **Group (1):** 30 healthy subjects (Control) matched for age and sex with patients groups (19 females, 11 males, mean age: 36.9 ± 8.9 years) between January 2017 and November 2019, **Group (2):** Renal transplant (Rtx) patients (16 females, 14 males; mean age: 40.0 ± 13.3 years), and group (3) 30 patients on Hemodialysis (HD) (18 females, 12 males; 46.6 ± 10.7 years) followed at least 6 months in the transplantation and dialysis units of El Maadi Military Hospital and All patients enrolled in the study were randomly assigned. Rtx patients received their grafts and dialysis patients received HD treatments at least 6 months prior to the study. All patients and control were recruited from El Maadi Military Hospital.

The study protocol was approved by the Medical Ethics Committee of Al Azhar University (Cairo faculty of medicine). Written informed consent was obtained from all subjects included in the study.

Inclusion criteria:

- Patients with chronic renal failure on regular hemodialysis for at least six months back.
- Stable patients who received renal transplant for at least six months back.
- Apparently healthy volunteers matching patients' group regarding age and sex.
- Age > 18 years.

Exclusion criteria:

- Diabetics.
- Elderly above sixty years.
- Patients with heart failure / Angina pectoris and/or documented coronary artery disease.
- Patients with active infection, or autoimmune disease.
- Patients with secondary hyperparathyroidism (PTH higher than 500 pg.).
- Patients with severe other comorbid conditions.

The following data were collected from patients and controls:

- Complete medical history with special stress on the cause of chronic renal failure and presence of other comorbid conditions.
- Clinical examination including systolic, diastolic, mean, and pulse pressure. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) of patients and healthy subjects were measured in the upright sitting position after 5 min of rest using a mercury sphygmomanometer. Two readings were recorded for each individual. The mean value of two readings was defined as the blood pressure. Patients with SBP 140 mm

Hg and DBP 90 mm Hg were assumed to be hypertensive.

Laboratory data included:

- White blood cell count (total, neutrophil, and lymphocyte count).
- Serum creatinine, and creatinine clearance by MDRD method for patients in group two and three.
- Blood lipid profile (S cholesterol, serum triglyceride, serum LDL and HDL).
- Serum calcium, phosphorus, and calcium phosphor product.
- C reactive protein.
- Serum iPTH.
- Serum Pentrixin - 3 (just before hemodialysis for patients in group one).
- Carotid intima and media thickness by duplex study for all subjects.

Statistical analysis of data:

The collected data was organized, tabulated and statistically analyzed using Statistical Package for Social Science (SPSS) version 18 (SPSS Inc, Illinois, Chicago, USA). For quantitative data, mean, standard deviation (SD), minimum and maximum were calculated Statistical differences between parametric data of three groups were analyzed using the analysis of variance (ANOVA) test. The Kruskal–Wallis test was used to determine differences between nonparametric data. The nonparametric Spearman coefficient of correlation was used to assess correlations between variables without normal distribution. For qualitative (categorical data), frequency and percent distribution were calculated, and for comparison between groups, the Chi square (X2) was calculated. P value < 0.05 was considered significant.

RESULTS

In the present study, patient age ranged from 30 to 59 years, and there was no significant difference between HD, Renal transplant group and control groups (50.07±5.14, 48.57±6.53 and 49.30±6.67 years respectively) **(Table 1)**.

Table (1): Comparison between studied groups as regard to age distribution

Age	Mean	S. D	Min.	Max.	p
Control group	49.30	6.67	30.00	59.00	0.64
Group I	50.07	5.14	39.00	57.00	
Group II	48.57	6.53	32.00	58.00	
Group III	49.31	6.11	30.00	59.00	

The present work included 90 subjects (30 in each group); there was 51 (56.7%) males and 39 (43.3%) females and there was no significant difference between HD, RT and control groups (males represented 56.7%, 60.0% and 53.3% in HD, RT and control groups respectively) **(Table 2)**.

Table (2): Comparison between studied groups as regard to sex distribution

		Groups						Total	
		Control group		Group III		Group II			
		n	%	n	%	n	%	n	%
Sex	Male	16	53.3%	17	56.7%	18	60.0%	51	56.7%
	Female	14	46.7%	13	43.3%	12	40.0%	39	43.3%
Statistics		X2 = 0.27, p = 0.83							
P1		0.059#		0.107#					
P2		**0.006**#							

= non-significant difference between RT, HD and controls groups; and # = non-significant difference between HD and RT(renal transplant) groups. p1: Statistical significance from control group (group 1), p2: Statistical significance between group RT, and HD group.

There was significant difference between HD, and RT patients as regard to duration of dialysis (30.33±16.14, and 20.8±6.8 months respectively) **(Table 3)**.

Table (3): Comparison between studied groups as regard to duration of dialysis

	Mean (month)	S. D (month)	p
HD group	30.33	±16.14	0.001
RT group (before of RT)	20.8	±6.8	

There was a significant difference between HD and control groups (P1). Also, there is significant difference between control group and RT (P2), non-significant difference between HD and RT group (P3). Regarding diastolic blood pressure for the studied groups there was significant difference between HD and control groups (P1). Also, there is non-significant difference between control group and RT(P2), non-significant difference between HD and RT group (P3) was also found **(Table 4)**.

Table (4): Comparison between studied groups as regard to systolic and diastolic blood pressure

		Mean	S. D	Min	Max	P1	P2	P3
Systolic	Group I	128.33	6.99	115.00	140.00			
	Group III	136.17*	8.48	120.00	150.00	**<0.005**		**0.0214**
	Group II	134.83#	5.00	125.00	140.00		**<0.005**	
Diastolic	Group I	80.17	5.17	70.00	95.00			
	Group III	84.83*	5.49	75.00	95.00	**<0.005**		**0.0095**
	Group II	82.67	5.68	70.00	90.00		**0.017**	

* = Significant difference between HD and control groups, while # = significant difference between RT and controls groups; and $ = significant differed between HT and RT groups. p1: Statistical significance between group HD, and control group (group 1), p2: Statistical significance between group RT, and control group, p3: Statistical significance between group RT, and HD group,

There was a significant difference between HD and control groups (P1). Also, there is non-significant difference between control group and RT (P2), non-significant difference between HD and RT group (P3). For pulse pressure the difference was significant in. P1, p3 but insignificant for P2.

Regarding TLC there was a significant difference between HD and control groups (GI). Also, there is significant difference between control group and RT (GI), significant difference between HD and RT group (GII). The same was also applied for lymphocytic count and neutrophil to lymphocytic ratio for the studied groups. Of notice, all are higher in HD group, while in RT group the mean lied in the intermediate position.

There was a significant difference between HD and control groups (P1). Also, there is significant difference between control group and RT (P2), significant difference between HD and RT group (P3). The same. significant difference was also applied for blood urea **(Table 5)**.

Table (5): Comparison between studied groups as regard to mean arterial, pulse pressure total leukocytic count, neutrophils and lymphocytic count, neutorphil lymphocyte ratio, serum creatinine, and urea

		Mean	S. D	Min	Max	P1	P2	P3
MAP	Control group	96.22	4.53	85.00	103.00			
	HD group	101.94*	5.57	91.00	113.00	**<0.005**		**0.351**
	RT group	100.06#	4.72	90.00	106.00		0.257	
Pulse pressure	Control group	48.17	7.82	25.00	60.00			
	HD group	51.33*	7.65	40.00	65.00	0.0018		**<0.005**
	RT group	52.17#	5.83	40.00	65.00		0.324	
TLC	Control group	4.95	0.52	4.10	6.50			
	HD group	9.54*$	1.84	6.70	15.80	**<0.005**		**<0.005**
	RT group	7.32#	0.88	5.40	8.90		**<0.005**	
Neutrophil	Control group	2.34	0.36	1.80	3.20			
	HD group	5.64*$	0.80	4.10	7.00	**<0.005**		**<0.005**
	RT group	4.09#	0.62	2.30	5.50		**<0.005**	
Lymphocyte	Control group	2.12	0.10	2.00	2.40			
	HD group	2.85*$	0.78	1.50	5.50	**<0.005**		**<0.005**
	RT group	2.25	0.19	2.00	2.60		**<0.005**	
N/L ratio	Control group	1.1	1.25					
	HD group	1.98	1.8			**<0.005**		<0.005
	RT group	1.82	1.31				**<0.005**	
Creatinine	Control group	0.65	0.18	0.30	1.00			
	HD group	6.95*	0.87	5.50	8.50	**<0.005**		**<0.005**
	RT group	1.37#	0.27	0.90	2.10		**<0.005**	
Urea	Control group	21.47	3.08	16.00	30.00			
	HD group	93.80*	10.42	80.00	120.00	**<0.005**		**<0.005**
	RT group	47.57#	6.45	35.00	60.00		**<0.005**	

* * = Significant difference between HD and control groups, while # = significant difference between RT and controls groups; and $ = significant differed between HT and RT groups. p1: Statistical significance between group HD, and control group (group 1), p2: Statistical significance between group RT, and control group , p3: Statistical significance between group RT, and HD group.

There was a significant difference between HD and control groups (P1). Also, there is significant difference between control group and RT (P2), significant difference between HD and RT group (P3). There was a significant difference between HD and control groups (P1). Also, there is significant difference between, between HD and RT group (P3). But there was non-significant difference between control group and RT (P2). There was a significant difference between HD and control groups (P1). Also, there is significant difference between control group and RT (P2), significant difference between HD and RT group (P3). There was a significant difference between HD and control groups (P1). Also, there is significant difference between control group and RT (P2), significant difference between HD and RT group (P3) **(Table 6)**.

Table (6): Comparison between groups as regard to iPTH, C–reactive protein, PTX3 and carotid intimal media thickness.

		Mean	S D	Min	Max	P1	P2	P3
iPTH	Control group	23.49	10.53	13.60	42.8			
	HD group	122.63	13.85	79.00	164.00	**<0.005**		**<0.005**
	RT group	43.91	9.28	32.50	77.45		**<0.005**	
CRP	Control group	1.3	0.25	1.15	2.3			
	HD group	9.43	0.91	6.50	15.20	**<0.005**		**<0.005**
	RT group	1.15	0.31	0.70	1.90		0.0287	
PTX3	Control group	1.00	0.35	0.50	1.80			
	HD group	5.18	1.62	1.80	5.82	**<0.005**		**<0.005**
	RT group	2.39	0.14	0.80	2.70		**<0.005**	
CIMT	Control group	0.55	0.11	0.50	0.70			
	HD group	0.85	0.02	0.80	0.90	**<0.005**		**<0.005**
	RT group	0.72	0.03	0.61	0.88			

DISCUSSION

In the present study, patient age ranged from 30 to 59 years, and there was no significant difference between HD, Renal transplant group and control groups (50.07±5.14, 48.57±6.53 and 49.30±6.67 years respectively). Similar age ranges were recorded by *Lavín-Gómez et al. (2011)*, they revealed that age ranged from 33 to 62 years with no significant difference between RT and control groups.

As regarding to gender, the present work included 90 subjects (30 in each group); there was 51 (56.7%) males and 39 (43.3%) females and there was no significant difference between HD, RT and control groups (males represented 56.7%, 60.0% and 53.3% in HD, RT and control groups respectively). Similar results were recorded by Turkmen et al. (2012), who found no significant difference between HD, RT and control groups as regard to gender.

In the present study, there was significant difference between HD, and RT patients as regard to duration of dialysis (30.33±16.14, and 20.8±6.8 months respectively). Similar duration of dialysis was recorded by *Argani et al. (2012)* who found significant difference between HD, and RT patients as regard to duration of dialysis (30.33±17.2 and 20.8±7.2 months respectively).

In the present work, PTX3 ranged from 0.50 to 10.20 and there was significant increase in RT group (2.39±1.14) and HD group (5.18±1.62) when compared to control group (1.00±0.35). In addition, there was significant decrease in RT when compared to HD group.

Furthermore, *Matsui et al. (2012)* reported that, PTX3 is increased in HD patients and has been suggested to induce vascular calcification and enhance cardiovascular mortality in these patients.

Also, this finding was supported by *Zhou et al. (2013),* who showed the ability of PTX-3 to bind to the C1q component of the complement cascade and to participate in the clearance of apoptotic cells; hence suggesting an important role for PTX-3 in the regulation of inflammatory reactions and innate immunity. In addition, because PTX-3 is produced from vascular endothelial cells and macrophages, PTX-3 levels may directly reflect the inflammatory status.

In addition, *El Sebai et al. (2016)* reported that, plasma PTX-3 demonstrated higher levels among CKD group as compared to controls.

In the contrary to the results of the present study, *Argani et al. (2012)* in an interesting study reported that, RT recipients had significantly higher plasma PTX3 concentration than HD patients.

The reasons for increased PTX3 levels in HD patients can be low grade inflammatory response due to incompatibility of dialysis membrane tissue, contamination of dialysis and endothelial damage, which results in the production of PTX3 from various immune cells, especially vascular endothelial cells *(Sjoberg et al., 2012).*

PTX3 can also be produced from oxidized LDL from vascular endothelial cells, which indicates the direct interference of inflammatory factors on blood vessels. Thus, PTX3 can be strongly expressed in vascular cells and atherosclerotic vascular inflammatory cells, as well as in patients with heart failure *(Kunes et al., 2012).*

As regard to kidney functions in our study, serum creatinine, was significantly differe between HD and control groups (P1). Also there was significant difference between control group and RT (P2), significant difference between HD and RT group (P3). The same significant difference was also applied for blood urea.

Similar to results of the present study *El Sebai et al. (2016)* agreed with us, they reported that, there was a significant difference between the three groups as compared to each other regarding serum urea, Hb, and plasma PTX-3 ($P < 0.001$), while a non-significant difference was found between the three groups as regards age and sex ($P > 0.05$). Meanwhile, a significant difference was found regarding serum creatinine in control group when compared to either HD or ESRD patient groups ($P < 0.001$).

This study shows that PTX3 levels are markedly increased also in patients with CKD. Similarly, a previous study by *Boehme et al., (2010)* revealed that PTX3 levels are markedly elevated in HD patients.

Regarding CRP, there was a significant difference between HD and control groups (P1). Also, there is significant difference

between, between HD and RT group (P3). But there was non-significant difference between control group and RT (P2).

Malaponte et al. (2010) also demonstrated no correlation exists between PTX3 and CRP in HD and uremic patients. Their study also showed that PTX3 is a more reliable marker for inflammation than CRP alone.

Also, *Lavín–Gómez et al. (2011),* found that serum CRP was increased in CKD patients.

We observed an association between PTX3 levels and the CRP levels. The hypothesis that the association between CRP and atherosclerosis is not only an association, but that CRP might directly promote atherosclerosis, has recently been reinforced by the observation that inhibition of CRP may reduce the extent of myocardial infarction in rats

Whereas some previous clinical studies found a weak or NS correlation between levels of PTX3 and CRP *(Mills et al., 2015).*

These contradiction of previous results to that of the present work could be attributed to different inclusion criteria and different study designs.

In addition, PTX-3 may have a more stable course than CRP, the protein PTX-3 may reflect disease activity directly. So, the correlation between CRP and PTX-3 may be weak or not significant *(Kovacs et al., 2010).*

It has been suggested that PTX3 plays the same role as CRP, the first denoting the tissue and the second denoting systemic inflammation *(Cozzolino et al., 2010).*

Multiple studies have reported a negative correlation between the PTX3 concentrations in plasma and kidney function *(Dubin et al., 2012).*

Furthermore, *Deban et al. (2011)* reported that PTX-3 could have a role in dampening excessive neutrophil recruitment, which may lessen inflammation. All of these findings were strengthened by the observation that PTX-3 deficiency is also associated with increased atherosclerosis and macrophage infiltration in these atherosclerotic lesions in apolipoprotein E-deficient mice *(Norata et al., 2010).*

Pentraxin-3 (PTX3) is an acute inflammatory marker and a vital component of innate immunity. Pathogens stimulate pentraxin-3 production in different cells including epithelial, endothelial, myeloid dendritic cells, neutrophils and macrophages. Pentraxin-3 promotes the recruitment of neutrophils *(Saleh et al., 2019).*

In the present work, CIMT, was in a significant difference between HD and control groups (P1). Also, there is significant difference between control group and RT (P2), significant difference between HD and RT group (P3).

In agreement to our study, *Hurst et al. (2010),* used ultrasound determination of CIMT as a marker of atherosclerosis as it was found to be a well-validated marker of atherosclerosis as well as a commonly used surrogate endpoint in clinical trials.

Similarly, Men had significantly higher mean CIMT compared with women (0.7056±0.1236 mm vs 0.6141±0.1167 mm, P=0.003), and subjects with CVD had higher CIMT values than those

without CVD (0.7288±0.1152 mm vs 0.6494±0.1272, P=0.026) *(Feldreich et al., 2019)*.

Therefore, one might hypothesize that Rtx may not completely reverse nontraditional risk factors including inflammation, oxidative stress, and atherosclerosis. The CIMT of our patients was also significantly high compared to healthy controls. Thus, by virtue of ongoing inflammation, our Rtx patients might have more atherosclerotic vessels than the controls. Assessment of the intima-media thickness (IMT) of the carotid artery is a reproducible, safe, and non-invasive method of detecting subclinical atherosclerosis.

Previous cross-sectional studies in cohorts without CKD have demonstrated associations between carotid IMT and both cardiovascular risk factors and the presence of CVD. Several large observational studies have also shown that carotid IMT is a predictor of coronary heart disease events that remains significant after adjustment for traditional risk factors *(Turkmen et al., 2012* and *Hurst et al., 2010)*.

In RT group, there was positive (proportional), significant correlation between PTX2 and each of CIMT, cholesterol, TG, LDL, creatinine clearance and calcium; while there was inverse (negative) correlation between PTX3 and HDL. In control group there were no correlation between PTX3 and the other variables.

There has been a debate regarding the exact role of PTX-3 in inflammation and atherosclerosis. Some researchers have suggested that PTX-3 might have a cardioprotective role as shown in a mouse model of acute myocardial infarction *(Boehme et al., 2010)*.

PTX3 modifies angiogenesis and atherosclerotic lesion development, and participates in extracellular matrix formation. High levels of PTX3 are associated with the presence of vulnerable coronary plaques, cardiovascular disease *(Gómez et al., 2020)*.

It has been shown that PTX3 is highly expressed in atherosclerotic lesions and in vascular cells exposed to inflammatory stimuli. Thereby, PTX3 level would predict atherosclerosis more correctly than the hsCRP level alone *(Mantovani et al., 2010)*.

In addition, PTX3 might be a predictor of cardiovascular disease, independent of traditional risk factors and of its homologous high-sensitivity CRP *(Knoflach et al., 2012)*.

In renal transplant patients, higher PTX3 levels have been found in comparison with those of healthy subjects, which suggest an ongoing inflammation, oxidative stress and atherosclerosis *(Turkmen et al., 2012)*.

Speeckaert et al. (2013) reported that, the described contradictory findings might be explained by the induction of different functions of PTX3 in various settings or temporal windows of vascular pathology.

Similar to the present study, *Turkmen et al., (2012)* revealed that both PTX-3 and hs-CRP levels were higher in Rtx patients compared to healthy subjects. Despite the improvement of kidney function in this population.

In addition, *Sjoberg et al. (2012)* introduced PTX3 as a sensitive initial

marker of inflammation associated with HD.

Therefore, it can be concluded that PTX3 is a more reliable and sensitive biomarker for inflammation compared to CRP and the absence of a correlation between PTX-3 and other inflammatory markers may be related to immunosuppressive drugs.

Therefore, Rtx patients might be considered a subset of CKD patients. This may partly explain why Rtx patients had high PTX-3 and hs-CRP levels.

Finally, Increased PTX-3 levels were observed in HD and RT patients in the present study. Our findings indicated that the plasma levels of PTX3 may serve as suitable biomarkers for CVD in HD and RT patients.

CONCLUSION

- Ptx-3 levels were significantly observed in HD and Rt patients when compared to control group. Serum profiles of pentraxin-3 and high sensitivity c - reactive protein in patients with chronic kidney disease treated with or without hemodialysiswere significantly observed.
- Pentraxin-3 was a more specific inflammatory vascular marker than C-reactive protein, and the best inflammatory marker associated with hemodialysis.
- There was a significant positive correlation between CIMT and Ptx-3 in patients on non-dialytic therapy and in patients on hemodialysis. There was proportional correlation between ptx-3 and CIMT both in HD and Renal transplant groups. In the same time, we found a significant decrease in its concentration after kidney transplantation.
- The plasma levels of PTX3 may server as suitable biomarkers for CVD in HD and RT patients.
- Pentraxin (PTX) family, were suggested as sensitive biomarkers to predict the development and progression of atherosclerosis.

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مستوى البنتراكسين 3 بالدم و تعصد الشرايين فى مرضى الغسيل الدموى الكلوى المزمن المعاشين على الاستصفاء الدموى المتكرر أو غرس الكلى

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خلفيـــة البحـــث: يعـــد مـــرض الكلـــى المـــزمن مشـــكلة صـــحية عامـــة واســـعة الانتشـــار فـــي جميـــع أنحـــاء العـــالم. أظهـــرت العديـــد مـــن الدراســـات الارتبـــاط بـــين المؤشـــرات الحيويـــة للالتهـــاب الجهـــازي، مثـــل البـــروتين C وعامـــل نخـــر الـــورم ألفـــا والفيبرينـــوجين، مـــع انخفـــاض وظـــائف الكلـــى. يرتفـــع البنتراكســـين 3 فـــي مرضـــى غســـيل الكلـــى مقارنـــة بالضـــوابط الصـــحية ويعكـــس الخلـــل البطـــاني المـــرتبط بـــأمراض القلـــب والأوعيـــة الدمويـــة ومخـــاطر الوفـــاة. تـــرتبط مســـتويات البنتراكســـين 3 المســـتمرة المرتفعـــة بخطـــر الوفيات المرتفع في مرضى غسيل الكلى.

الهـــدف مـــن البحـــث: صـــممت هـــذه الدراســـة لمعرفـــة مســـتوى مصـــل البنتراكســـين فـــي المرضى الذين يخضعون لغسيل الكلى المنتظم والذين يخضعون لزراعة الكلى.

المرضـــى وطـــرق البحـــث: كانـــت دراســـة حالـــة ضـــابطة، والتـــي شـــملت 30 مريضًـــا يعـــانون مـــن الفشـــل الكلـــوي المـــزمن تحـــت غســـيل الكلـــى المنـــتظم لمـــدة ســـتة أشـــهر علـــى الأقـــل (مجموعـــة غســـيل الكلـــى)، وثلاثـــين مريضًـــا لـــديهم زراعـــة كلـــى مســـتقرة والـــذين تلقـــوا عمليـــة الـــزرع لمـــدة ســـتة أشـــهر علـــى الأقـــل (مجموعـــة زرع الكلـــى) و ثلاثـــون عنصـــر تحكـــم ســـليم ظاهريًـــا مطابقـــة للعمـــر والجـــنس مـــع مجموعـــات المرضـــى (المجموعـــة الضـــابطة). تـــم اســـتقدام جميـــع المرضـــى والشـــواهد مـــن مستشـــفى المعـــادى العسكرى من يناير 2017 وحتي نوفمبر 2019.

نتـــائج البحـــث: تـــم زيـــادة ضـــغط الـــدم، العـــدد الكلـــي لتخثـــر الـــدم، العـــدلات، الخلايـــا الليمفاويـــة، الكريـــاتينين، اليوريـــا، الكوليســـترول، الفوســـفور، منـــتج الكالســـيوم والفوســـفور والبـــروتين التفـــاعلي بشـــكل ملحـــوظ فـــي مجموعـــات المرضـــى بالمقارنـــة

مع المجموعة الضابطة. تراوحت بينتراكسين -3 من 0.50 إلى 10.20 وكان هناك زيادة معنوية في مجموعة غسيل الكلى (2.39 ± 1.14) ومجموعة زرع الكلى (5.18 ± 1.62) بالمقارنة مع مجموعة التحكم (1.00 ± 0.35). بالإضافة إلى ذلك، كانت هناك زيادة معنوية في زرع الكلى بالمقارنة مع مجموعة الدم. تراوحت سماكة الشريان السباتي من 0.4 إلى 0.88 وكان هناك زيادة معنوية في سمك الشريان السباتي في غسيل الكلى (0.85 ± 0.02) ومجموعة زرع الكلى (0.84 ± 0.03) بالمقارنة مع مجموعة التحكم (0.55 ± 0.11)؛ لكن الفرق بين مجموعات غسيل الكلى ومجموعات زرع الكلى كان غير معتد به إحصائياً. في مجموعة غسيل الكلى، كان البنتراكسين مرتبطا إيجابيا مع سمك الشريان السباتي والكوليسترول و LDL وارتبط عكسيا مع مجموع الليوكوسيك COUNT. في مجموعة زرع الكلى كان هناك ارتباط موجب ومعنوي بين البنتراكسين وكل من سمك الشريان السباتي والكوليسترول و TG و LDL وتصفية الكرياتينين والكالسيوم. بينما كان هناك ارتباط عكسي (سلبي) بين البنتراكسين وغسيل الكلى.

الاستنتاج: قد تكون مستويات البلازما للبنتراكسين 3 بمثابة مؤشرات حيوية مناسبة لأمراض القلب والأوعية الدموية في غسيل الكلى ومرضى زرع الكلى.

الكلمات الدالة: البنتراكسين 3، تصلب الشرايين، أمراض الكلى المزمنة، غسيل الكلى، استبدال الكلى.