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Serum Profiles of Pentraxin-3 and High Sensitivity C - Reactive Protein in Patients with Chronic Kidney Disease Treated with or without Hemodialysis

EL-Attar HA[1*], Abaza MM[1], Gaber EW[2] and EL-sharkawy RM[1]

[1]*Chemical Pathology Department, Medical Research Institute, University of Alexandria, Israel*

[2]*Internal Medicine Department, Medical Research Institute, University of Alexandria, Israel*

[*]**Corresponding author:** EL-Attar HA, Medical Research Institute, University of Alexandria, Israel, Tel: +201020244286; E-mail: hoda.ali55151@yahoo.com

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Abstract

Background: The first cloned long pentraxin is Pentraxin 3(PTX3) and C-reactive protein is a human short pentraxin. Pentraxin 3 has a bigger molecular size (40.6 kDA) compared to CRP (21.5 kDa).The long PTX3 is produced by diverse cell types in response to primary inflammatory signals and specific neutrophil granules store PTX3.

Aim: Evaluate serum levels of long pentraxin 3 and high sensitivity C-reactive protein in patients with chronic kidney disease treated with or without hemodialysis. The study included 75 subjects, 25 heathy controls (group 1), 50 patients without cardiovascular disease subdivided into: 25 patients with chronic kidney disease (CKD) on conservative therapy (group 2a) and 25CKD patients on maintenance hemodialysis (group 2b). To all studied subjects the following was done: electocardiography, carotid intima media thickness, fasting serum glucose, renal, liver and lipid profiles, high- sensitivity C-reactive protein (hsCRP) and PTX3by ELISA.

Results: There was a significant decrease in the mean levels of albumin in all the studied chronic renal failure patients when compared to controls. Hypoalbuminemia is due to malnutrition and inflammation in CKD patients. There was a significant increase in hsCRP in patients on hemodialysis therapy when compared to both controls and patients on non-dialytic therapy. The circulating value of CRP reflects ongoing inflammation and/or tissue damage. There was a significant increase in PTX3 in patients on hemodialysis therapy as compared to controls. PTX3 levels may directly reflect the inflammatory status. Since a state of persistant low-grade inflammation is a common feature in hemodialysis patients so PTX3 increased in such patients. There were no correlations between PTX3 and hsCRP in the studied groups. By drawing the ROC curve for hsCRP and PTX3 in patients on non-dialytic therapy (group 2a), the area under the curve was 0.545 (p=0.594) and 0.653 (p=0.073) respectively. In patients on hemodialysis therapy (group 2b), the area under the curve was 0.735 (p=0.006) for hsCRP and 0.765 (p=0.002) for PTX3. By using the best cut off values, it was found that high sensitivity C-reactive protein showed a better specificity and positive predictive value than PTX3 while PTX3 showed a better sensitivity than hsCRP in the studied two groups of patients.

Conclusion: It could be concluded that using both hsCRP and PTX3 complement each other to give better specificity and sensitivity as predictors of inflammation in chronic kidney disease patients.

Recommendation: Study of PTX3 and hsCRP on a large number of chronic kidney disease patients with cardiovascular disease.

Keywords: Chronic kidney disease; Pentraxins; Pentraxin 3; hsCRP; Hemodialysis

Introduction

Pentraxins are a superfamily of proteins highly conserved during evolution and characterized by a multimeric usually pentameric structure [1].

This family is subdivided into two subclasses, short and long pentraxins, that depend on the length and structure of the molecules. The classic short pentraxins, C-reactive protein (CRP) and Serum amyloid P (SAP) are acute phase proteins present in humans and mice respectively. They are produced in the liver in response to inflammatory signals, most prominently interleukin 6, which serves as a marker of inflammation and infection. Both could increase significantly during acute phase reaction [1,2].

The first cloned long pentraxin is Pentraxin 3, also was called tumor necrosis factor (TNF)-stimulated gene 14 [3]. Other long pentraxins identified in human are Pentraxin 4, Neuronal pentraxin 1and Neuronal pentraxin 2 [4].

PTX3 has a bigger molecular size (40.6 KD) compared to CRP (21.5 KD) [5]. PTX3 contains a unique PTX3 domain not found in CRP or SAP [6]. Long pentraxins are characterized by an unrelated N-terminal domain (amino acids 18-178) coupled to a short PTX-like C-terminal domain (amino acids 179-381) [7,8]. Carboxy-terminal domain

contains the canonical pentraxin signature of eight amino acids sequence (HxCxS/TWxS). PTX3 gene is organized in three exons encoding for 381 amino acids [9].

The long PTX3 is rapidly produced and released by diverse cell types, in particular by mononuclear phagocytes, dendritic cells, endothelial cells and epithelial cells in response to primary inflammatory signals (e.g. Toll-like receptor engagement, TNF-α and IL-1β), but is not a component of the classic acute phase response (systemic inflammation) [10,11]. PTX3 is mainly expressed extra-hepatically [3]. PTX3 is rapidly produced directly from damaged tissues and directly reflects the inflammatory state [12]. Different microorganisms (fungi- bacteria- viruses) may activate macrophages and dendritic cells through Toll-like receptors. These cells can produce PTX3. PTX3 could be a soluble factor for immediate innate response and influence the adaptive immunity [9,10]. In contrast to CRP, PTX3 showed little relationship with classic vascular risk factors and pro-inflammatory condition. It appears to be more specific for vascular inflammation [13].

PTX3 is stored in a ready-made form in neutrophils localized in specific granules, and secreted in response to recognition of microbial moieties and inflammatory signals. PTX3 can localize in neutrophil extracellular traps (NETs). Thus, neutrophils serve as a reservoir, ready for its rapid release. PTX3 usually form multimers with a discoid arrangement of five subunits. PTX3 assembles as a decamer and can be produced as 10-20 subunit multimer proteins [1,7].

PTX3 participates in the clearance of apoptotic cells and several microorganisms [3].

PTX3 may exert a dual role and contrasting effects on complement activation. It supports clearance of microbes recognized, facilitating recognition by phagocytes, whereas, on the other hand, it may protect against unwanted complement activation in the fluid phase [1].

PTX3 mRNA is expressed in normal human kidney. Stimulation with IL-1, TNF-α, IL-17 and CD40L increases the expression and production of PTX3 by renal epithelial cells [3].

The gradual increase of PTX3 concomitent to the decline in glomerular filtration rate (GFR) could be explained by an inadequate clearance because PTX3 is a large molecular weight substance (molecular weight 40.6 kDa) characterized by a multimeric, usually pentameric structure, but it could also be explained by an enhanced synthesis/release upon stimulation in peripheral tissues and also perhaps the decline in the remaining functioning kidney [5].

Serum levels of PTX3 are elevated in a number of human diseases, such as myocardial infarction, rheumatoid arthritis and sepsis and in other diseases such as small vessel vasculitis, inflammatory reaction in the kidney [3,14].

Chronic kidney failure is also referred to end-stage renal disease, is total or near-total loss of kidney function with glomerular filtration rate less than 15 ml/min/1.73m^2 and patients need replacements therapy in form of haemodialysis or kidney transplantation to substitute the lack of excretory kidney function [15].

End stage renal disease is defined as the need for renal replacement therapy (the need for dialysis or renal transplantation) [16].

Cardiovascular disease remains the major cause of morbidity and mortality in end-stage renal disease patients (ESRD) [2]. Individuals with CKD are more likely to die from cardiovascular disease than to develop kidney failure [16]. Some studies reported that about 39.8% of patients with ESRD undergoing dialysis develop cardiovascular disease [17]. Increased morbidity and mortality of dialysis patients due to cardiovascular diseases, and cardiovascular morbidity due to accelerated atherosclerosis is now considered a determinant of the prognosis of hemodialysis patients [18].

In ESRD, hs-CRP has been proven to be a strong predictor of both cardiovascular and all-cause mortality, and associated with oxidative stress, vascular calcification and endothelial dysfunction [19].

The present work aimed at evaluation of serum levels of long pentraxin 3 and high sensitivity C-reactive protein in patients with chronic kidney disease treated with or without haemodialysis.

Subjects

This study included 75 subjects, 25 healthy controls (group 1), 50 patients without cardiovascular disease subdivided into: 25 patients with chronic kidney disease (CKD) on conservative therapy (group 2a) and 25 CKD patients on maintenance hemodialysis (group 2b).

Methods

The procedures were in accordance with the ethical standards committee of MRI based on revised Helsinki Declaration. To all studied subjects the following was done electocardiography, carotid intima media thickness [20], fasting serum [21]: glucose ,renal, liver and lipid profiles, high- sensitivity C-reactive protein (hsCRP) and PTX3 [22] by ELISA. Statistical analysis [23,24] was done using the Predictive Analytic Software(PASW statistics 18) to obtain the mean, standard deviation. ANOVA was performed for comparison between more than 2 samples. Mann-Whitney test was used to test the significant difference between 2 groups. A p values less than 0.05 was considered statistically significant. Diagnostic sensitivity, specificity, predictive values to healthy and diseased people and ROC curve were performed.

Results

ECG findings were unremarkable in all the studied subjects.

There was a significance increase in CIMT in patients on non-dialytic therapy (group 2a) as compared to both controls and group 2b.

There was a significant increase in urea, creatinine and uric acid in patients on non-dialytic therapy (group 2a) and patients on hemodialysis (group 2b) as compared to control group (group 1). There was also significant increase in urea and creatinine in group 2b as compared to group 2a.

There was a significant decrease in the mean levels of albumin in all the studied chronic renal failure patients when compared to controls.

There was a significant decrease in serum cholesterol level in patients on non-dialytic therapy (group 2a) and patients on hemodialysis (group 2b) as compared to controls (group 1).

There was also a significant decrease in HDL-C in group 2a and group 2b as compared to control group (group 1).

There was a significant decrease in LDL-C in group 2b as compared to control group (group 1).

There was a significant increase in hsCRP in patients on hemodialysis therapy when compared to both controls and patients on non-dialytic therapy.

There was a significant increase in PTX3 in patients on hemodialysis therapy as compared to controls.

There were no correlations between PTX3 and hsCRP in the studied groups. By drawing the ROC curve for hsCRP and PTX3 in patients on non-dialytic therapy (group 2a), the area under the curve was 0.545 (p=0.594) and 0.653 (p=0.073) respectively. In patients on hemodialysis therapy (group 2b), the area under the curve was 0.735 (p=0.006) for hsCRP and 0.765 (p=0.002) for PTX3.

Discussion

The first cloned long pentraxin is pentraxin 3. Plasma pentraxin 3 level is elevated in critically ill patients, with a gradient from systemic inflammatory response to septic shock, and in several other diseases, such as myocardial infarction, atherosclerosis, vasculitis, lung disease, eclampsia, rheumatoid arthritis, psoriasis and chronic kidney disease [5,25-27].

	Control group		Patients on non-dialytic therapy		Patients on hemodialysis		Test of sig.
	(Group 1)		(Group 2a)		(Group 2b)		
	No.	%	No.	%	No.	%	
Male	4	16	10	40	9	36	p=0.143
Female	21	84	15	60	16	64	
p1			0.059		0.107		
p2			0.771				
Age							
Mean ± SD	35.56 ± 13.24		52.52 ± 8.01		49.88 ± 9.03		Fp<0.001*
Schp1			<0.001*		<0.001*		
Schp2			0.667				
CIMT(mm)							
Mean ± SD	0.64 ± 0.04		0.69 ± 0.05		0.66 ± 0.04		Fp=0.001*
Schp1			0.001*		0.555		
Schp2			0.023*				

Note: P: Statistical significance for comparing between the studied groups, χ2: Chi square test (for comparison of sex), p1: Statistical significance from control group (group 1), p2: Statistical significance between group 2a and group 2b, F: F test (ANOVA), Sch: Post Hoc Test (Scheffe), *: Statistically significant at p ≤ 0.05.

Table 1: Statistical significance between the studied groups according to demographic data and CIMT.

The prevalence of chronic kidney disease (CKD) is rising dramatically and is associated with markedly increased in-hospital morbidity and mortality [28]. Nauta et al. [8] showed that renal epithelial cells are able to produce PTX3. Pentraxin 3 may amplify the inflammatory response after being produced both in peripheral tissues and in the kidney, it may also play an important role in the atherogenic process present in CKD. Pentraxin 3 increased in early stages of renal damage in patients with diabetes even when GFR seems to be normal [29]. However, no enough studies have evaluated PTX3 in patients with chronic kidney disease.

	FSG (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)	U.A (mg/dl)	Albumin (g/dl)	ALT (U/L)
Control group						
(Group 1)						
Mean ± SD	84.44 ± 9.30	24.80 ± 6.74	0.87 ± 0.17	4.35 ± 0.99	4.43 ± 0.34	17.66 ± 8.12
Patients on non-dialytic therapy						
(Group 2a)						
Mean ± SD	88.56 ± 20.28	119.80 ± 33.58	5.94 ± 3.33	7.06 ± 1.46	3.63 ± 0.81	17.50 ± 13.87
Patients on hemodialysis						
(Group 2b)						
Mean ± SD	90.80 ± 26.10	163.16 ± 36.92	9.60 ± 2.83	7.46 ± 1.23	3.65 ± 0.46	17.32 ± 7.15
P	Fp=0.519	Fp<0.001*	KWp<0.001*	Fp<0.001*	Fp<0.001*	KWp=0.739
p1	Schp=0.764	Schp<0.001*	MWp<0.001*	Schp<0.001*	Schp<0.001*	MWp=0.593
p2	Schp=0.529	Schp<0.001*	MWp<0.001*	Schp<0.001*	Schp<0.001*	MWp=0.977
p3	Schp=0.923	Schp<0.001*	MWp=0.001*	Schp=0.513	Schp=0.989	MWp=0.425

p: Statistical significance for comparing between the different studied groups, p1: Statistical significance between Control group (group 1) and group 2a, p2: Statistical significance between group 1 and group 2b, p3 : Statistical significance between group 2a and group 2b, F: F test (ANOVA), Sch: Post Hoc Test (Scheffe), KW: Kruskal Wallis test, MW: Mann Whitney test, *: Statistically significant at p ≤ 0.05.

Table 2: Statistical significance between the studied groups for fasting levels of serum Glucose (FSG), Urea, Creatinine, Uric acid (U.A), Albumin and Alanine aminotransferase activity (ALT).

The present study included seventy five non-diabetic subjects and clinically free from cardiovascular manifestations. They are divided into two groups. The control group (group 1) included twenty five apparently healthy volunteers, 4 males (16%) and 21 females (84%). The patients group included fifty patients with CKD which was subdivided into two subgroups (group 2a) included twenty five patients with CKD on non-dialytic therapy, 10 males (40%) and 15 females (60%) and (group 2b) included twenty five hemodialysed patients, 9 males (36%) and 16 females (64%).

Carotid intima media thickness (CIMT) is a surrogate marker for atherosclerosis and can be used to detect an accelerated disease process and subclinical disease [30]. The mean level of CIMT in control group was 0.64 ± 0.04 mm while in (group 2a), it was 0.69 ± 0.05 mm and in (group 2b), CIMT was 0.66 ± 0.04 mm. Although, there was a significant increase in CIMT in (group 2a) as compared to both control group and group 2b (Table 1), the mean values of CIMT were within the normal range (0.52 mm to 0.95 mm) for all the studied groups [30].

In the present study, there was a significant increase in urea, creatinine and uric acid ($p<0.001$ for all) in patients on non-dialytic therapy and patients on hemodialysis therapy as compared to control group, and between group 2a and group 2b, for urea and creatinine (Table 2). Increased concentrations of nitrogenous compounds in plasma, such as urea and creatinine, is due to reduced glomerular filtration rate and decreased tubular function [21].

	Cholesterol (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	TG (mg/dl)
Control Group				
(Group 1)				
Mean ± SD	155.76 ± 19.56	53.20 ± 9.92	88.19 ± 20.78	71.88 ± 28.51
Patients on non-dialytic therapy				
(Group 2a)				
Mean ± SD	136.12 ± 26.69	36.92 ± 10.07	74.54 ± 28.89	85.04 ± 24.03
Patients on hemodialysis				
(Group 2b)				
Mean ± SD	125.40 ± 26.98	39.78 ± 10.03	68.66 ± 25.21	84.64 ± 24.52
P	<0.001*	<0.001*	0.023*	0.129
p1	0.023*	<0.001*	0.166	0.203
p2	<0.001*	<0.001*	0.028*	0.223
p3	0.313	0.602	0.713	0.998

p: Statistical significance, F test (ANOVA) for comparing between the different studied groups, p1: Statistical significance between group 1 and group 2a (Post Hoc Test -Scheffe), p2 : Statistical significance between group 1 and group 2b (Post Hoc Test –Scheffe), p3 : Statistical significance between group 2a and group 2b (Post Hoc Test – Scheffe), *: Statistically significant at p ≤ 0.05.

Table 3: Statistical signficance between the studied groups according to fasting serum levels of Cholesterol (mg/dl), High density lipoprotein cholesterol (HDL-C) (mg/dl), Low density lipoprotein cholesterol (LDL-C) (mg/dl) and Triglycerides (mg/dl).

The mean level of serum albumin in control group was 4.43 ± 0.34 g/dl while in patients on non-dialytic therapy (group 2a) was 3.63 ± 0.81 g/dl and in patients on hemodialysis therapy (group 2b) was 3.65 ± 0.46 g/dl. There was a significant decrease in serum albumin in patients in group 2a and patients in group 2b as compared to control group. This goes in agreement with the results of other studies as Tong et al. [31] found albumin in non-dialytic patients was 3.7 ± 0.3 g/dl and in hemodialysis patients was 3.3 ± 0.6 g/dl. Suliman et al. [29] found albumin was 3.3 ± 0.6 g/dl in patients with stage 5 CKD. Hypoalbuminemia in CKD patients results from many causes including malnutrition [32], due to decrease in protein intake and anorexia, acidosis, loss of nutrients and endocrine disorders as insulin resistance [32]. In addition, albumin being an acute phase protein that decreases in inflammatory conditions which presents in renal failure patients. Low levels of serum albumin are highly predictive of poor clinical outcomes in all stages of CKD [21].

In the present work, there was a significant decrease in the mean levels of cholesterol and HDL-C in group 2a and group 2b as compared to controls and in the mean level of LDL-C in group 2b as compared to both controls and group 2a (Table 3). LDL-C and cholesterol levels are decreased due to malnutrition and diet restriction [32], while HDL-C is decreased due to decreased activity of hepatic lipase and lipoprotein lipase enzymes caused by accumulation of toxins with inhibitory effect in CKD patients [33].

In this work, the levels of hsCRP in the control group ranged from 0.11 mg/L to 8.46 mg/L with a median value of 7.05 mg/L, as reported in other previous studies, Suliman et al. [29] found that hsCRP ranged from 0.2 mg/L to 32.0 mg/L with a median of 1.2 mg/L . Kanbay et al. [34] found that mean value ± SD of hsCRP level in control group was 3.5 ± 2.6 mg/L and was 1.69 ± 2.68 mg/L by Jenny et al. [35].

	CRP (mg/L)	PTX3 (ng/ml)
Control group		
(Group 1)		
Min. – Max.	0.11 – 8.46	20.79 – 26.16
Median	7.05	22.99
Patients on non-dialytic therapy		
(Group 2a)		
Min. – Max.	0.07 – 15.03	21.41 – 100.04
Median	4.84	23.62
Patients on hemodialysis		
(Group 2b)		
Min. – Max.	0.15 – 30.78	22.04 – 40.56
Median	11.4	24.25
P	0.011*	0.009*
p1	0.502	0.072
p2	0.005*	0.002*
p3	0.025*	0.165

p: Statistical significance, Kruskal Wallis test for comparing between the different studied groups, p1 : Statistical significance between group 1 and group 2a (Mann Whitney test), p2 :Statistical significance between group 1 and group 2b (Mann Whitney test), p3: Statistical significance between group 2a and group 2b (Mann Whitney test), *: Statistically significant at p ≤ 0.05.

Table 4: Statistical significance between the studied groups according to serum levels of C-reactive protein and Pentraxin3.

In the present study, in patients on non-dialytic therapy (group 2a), hsCRP levels ranged from 0.07 mg/L to 15.03 mg/L with a median value of 4.84 mg/L, showing no statistic significant difference when compared to controls (Table 4). In previously reported values by Tong et al. [31], they found that CRP ranged from 0.3 mg/L to 49 mg/L with a median value of 2.8 mg/L and Suliman et al. [29] also found that CRP ranged from 0.2 mg/L to 218.0 mg/L with a median range of 4.3 mg/L.

In this study, the values of hsCRP in hemodialysis patients (group 2b) ranged from 0.15 mg/L to 30.78 mg/L with a median value of 11.40 mg/L (Table 4). There was a significance increase in hsCRP in hemodialysis patients (group 2b) when compared to both controls (p=0.005) and group 2a (p= 0.025) (Table 4).

The circulating value of CRP reflects ongoing inflammation and/or tissue damage [36]. The inflammatory response strongly promotes the production of acute-phase proteins such as CRP and pro-inflammatory cytokines, when combined with malnutrition, which is more common in patients with chronic inflammation, it predicts poor outcome. Thus, malnutrition, inflammation and atherosclerosis (MIA) syndrome is the major risk factor for premature death in patients with ESRD. The hemodialysis procedure itself contributes to the inflammatory response. The possible contributing factors are the presence of catheter, graft, fistula infection, contamination of dialysis fluid, back filtration and back diffusion of contaminated dialysate, and the use of bio-incompatible membranes [37]. Increase in CRP during the HD session was associated with an increased mortality risk [38]. In CKD, there is chronic inflammation and patients with CKD but not yet on dialysis are also at increased mortality risk, but their hsCRP concentrations are lower than that in patients with ESRD [37].

	CIMT	
	r	**p**
Age	0.624*	0.001

Table 5a: Significant correlations in patients on non-dialytic therapy (group 2a).

	r	**p**
CIMT and age	0.693*	<0.001
CRP and TG	0.412*	0.041
CRP and LDL-C	-0.537*	0.006

Table 5b: Significant correlations in patients on hemodialysis (group 2b).

There was a positive correlation between hsCRP and TG (r=0.412 and p=0.041) and a negative correlation between hsCRP and LDL-C in patients on hemodialysis therapy (r=-0.537 and p=0.006) (Tables 5a and 5b). In CKD, there is chronic inflammation where LDL-C decrease with inflammation, while CRP increase in inflammation [39]. However, we could not find any significant correlation between hsCRP and PTX3 in the studied groups (Table 5c).

Pentraxin 3 is a candidate marker for inflammatory, infectious and cardiovascular pathologies. PTX3 behaves as an acute-phase protein since its blood levels, low in normal conditions and increase rapidly (with a maximum at 6-8 hours) and dramatically (200-800 ng/ml) during endotoxic shock, sepsis, and other inflammatory and infectious conditions [10,40].

Systemic levels of PTX3 also increase as renal function declines and predict increased cardiovascular and overall mortality risk in CKD patients [41]. PTX3 may be superior to CRP as an independent predictor of underlying atherosclerosis in subjects with CKD [42].

In the present study, the levels of PTX3 in the controls ranged from 20.79 ng/ml to 26.16 ng/ml with a median value of 22.99 ng/ml (Table 4). Tong et al. [31] found that PTX3 in their controls ranged from 0.1 ng/ml to 9.1 ng/ml with a median value of 1.8 ng/ml. Yilmaz et al. [43] found that PTX3 in their study ranged from 0.1 ng/ml to 2.7 ng/ml with a median value of 1.3 ng/ml. Nishi et al. [44] found that PTX3 in their study was 2.15 ng/ml ± 0.93 ng/ml.

CRP						
Control Group			**Patients on non-dialytic therapy**		**Patients on hemodialysis**	
(Group 1)			(Group 2a)		(Group 2b)	
	rs	p	rs	p	rs	p
PTX3	-0.042	0.854	0.286	0.166	-0.28	0.175

Table 5c: Correlation between CRP and PTX3 in each studied group. rs: Spearman coefficient. There was no significant correlation between CRP and PTX3 in the studied groups.

In the present work, in patients on non-dialytic therapy, PTX3 levels ranged from 21.41 ng/ml to 100.04 ng/ml with a median value of 23.62 ng/ml. There was non-significant increase in PTX3 values in this group when compared to control group (Table 4). Tong et al. [31] found that in CKD patients at stage 3-4, PTX3 was 2.2 ng/ml (ranging from 0.4 ng/ml to 16 ng/ml) and incident dialysis CKD stage 5 patients was 5.7 ng/ml (ranging from 0.9 ng/ml to 64.3 ng/ml). Another previous value for PTX3 were reported by Suliman et al. [29], PTX3 ranged from 1.0 ng/ml to 58.0 ng/ml with a median value of 5.3 ng/ml and by Yilmaz et al. [43], PTX3 ranged from 1.8 ng/ml to 32.9 ng/ml with a median value of 7.7 ng/ml. Also, Nishi et al. [44], found that PTX3 had a mean value of 3.80 ± 2.35 ng/ml and in Pradeep et al. [45], it was 5.4 ± 2.65 ng/ml.

In this work, the values of PTX3 in patients on hemodialysis therapy (group 2b) ranged from 22.04 ng/ml to 40.56 ng/ml with a median value of 24.25 ng/ml. (Table 4). Previously reported PTX3 mean values on hemodialysis patients, by Malaponte et al. [46] was 3.03 ± 1.81 ng/ml. Xu et al. [47] found that PTX3 ranged from 1.34 ng/ml to 2.50 ng/ml with a median value of 1.87 ng/ml and by Argani et al. [41], PTX3 ranged from 0.24 ng/ml to 7.89 ng/ml with a median value of 1.65 ng/ml.

The difference in our values compared to other previously reported values may be attributed to difference in the assay method used and different populations studied.

In the present work, there was a significant increase in PTX3 in group 2b as compared to control group (p=0.002) (Table 4). Similarly, previous studies [31,29] found significant increase in PTX3 levels in patients on hemodialysis therapy when compared to controls (p<0.001). Tong et al. [31] found that the hemodialysis patients had significantly higher median PTX3 concentration of 10.6 ng/ml with a range of 2.4 ng/ml to 75.1 ng/ml when compared to control subjects and Suliman et al. [29] found that hemodialysis patients had median PTX3 concentration of 5.3 ng/ml with a range of 1.0 ng/ml to 58.0 ng/ml.

Pentraxin 3 is induced by TNF-α or IL-1 in multiple human tissue cells as vascular endothelial cells and macrophages, PTX3 levels may directly reflect the inflammatory status. Since a state of persistent low-grade inflammation is a common feature in hemodialysis patients so PTX3 increased in such patients. Researchers found that a single hemodialysis session increased PTX3, and that this rise was not associated with changes in CRP or IL-6 [25,39]. There are also increases of PTX3 due to exposure of tissues to diversity of inflammatory stimuli induced by uremic milieu [25]. The bigger molecular size of PTX3 (40.6 KD) may suggest increased retention in uremia so its level increased in patients with impaired renal functions [29,31].

From the majority of previous studies, pentraxin 3 levels were increased in patients with CKD when compared to healthy controls. They stated that elevated PTX3 levels were associated with the presence of cardiovascular disease. Increase inflammatory markers as PTX3, reflect tissue damage, therefore, they may represent the degree of severity of cellular or organ damage. There is association between PTX3 and co-morbidities as inflammatory markers may reflect the presence of co-morbidity in CRF patients [25,31,34,48].

By drawing the ROC curve for hsCRP and PTX3 in patients on non-dialytic therapy (group 2a), the area under the curve was 0.545 (p=0.594) and 0.653 (p=0.073) respectively (Figure 1). In patients on hemodialysis therapy (group 2b), the area under the curve was 0.735 (p=0.006) for hsCRP and 0.765 (p=0.002) for PTX3 (Figure 2) denoting that PTX3 is a better indicator of inflammation in group 2b than hsCRP.

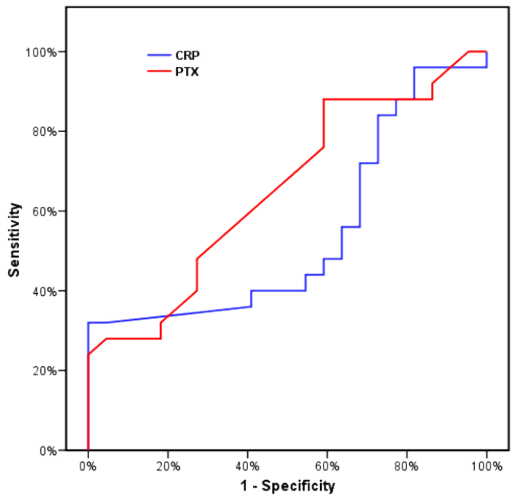

Figure 1: ROC curve for CRP and PTX3 in group 2a.

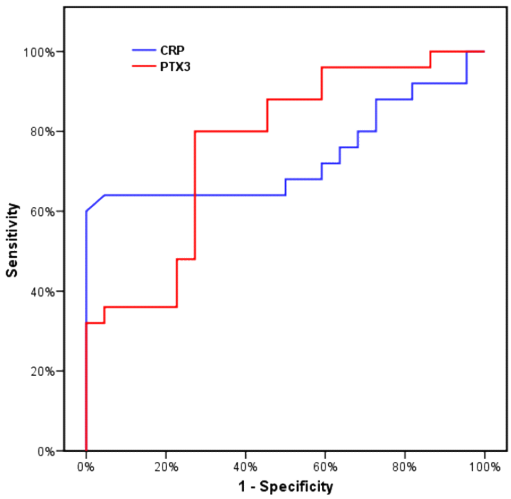

Figure 2: ROC curve for CRP and PTX3 in group 2b.

Using a cut off value of 8.46 mg/L in patients on non-dialytic therapy (group 2a), hsCRP had sensitivity of 40.0%, specificity of 100.0%, positive predictive value of 100.0%, negative predictive value of 62.50% and efficiency of 70.0%. In patients on hemodialysis therapy (group 2b), sensitivity was 60.0%, specificity was 100.0%, positive predictive value was 100.0%, negative predictive value was 71.43% and efficiency was 80.0%. This shows a better sensitivity, negative predictive value and efficiency for hsCRP in patients on hemodialysis therapy than non-dialytic therapy patients.

Using a cut off value of 22.36 ng/ml in patients on non-dialytic therapy (group 2a), PTX3 had sensitivity of 88.0%, specificity of 40.91%, positive predictive value of 62.86%, negative predictive value of 75.0% and efficiency of 65.96% showing a better sensitivity and negative predictive value than hsCRP. In (group2b), using a cut off of 23.62 ng/ml, PTX3 had sensitivity of 72.0%, specificity was 72.73%, positive predictive value was 75.0%, negative predictive value was 69.57% and efficiency was 72.34% showing a better sensitivity than hsCRP. However, hsCRP had a better specificity (100%) than PTX3 in both the two groups of patients.

Conclusions

There was a significant positive correlation between CIMT and age in patients on non-dialytic therapy and in patients on hemodialysis. Age induce intrinsic changes in the arterial wall including progressive increase in intimal thickness.

There was a significant decrease in serum albumin and HDL-C in all studied chronic renal failure patients when compared to controls. Hypoalbuminemia is due to malnutrition and inflammation in CKD patients while decreased HDL-C is due to decreased activity of hepatic lipase and lipoprotein lipase enzymes in CKD patients.

There was a significant increase in hsCRP in patients on hemodialysis therapy when compared to both controls and patients on non-dialytic therapy. The circulating value of CRP reflects ongoing inflammation and/or tissue damage.

There was a significant increase in PTX3 in patients on hemodialysis therapy (group 2b) as compared to control. PTX3 reflects the inflammatory status. Since a state of inflammation is common in hemodialysis patients so PTX3 was elevated.

There were no correlations between PTX3 and hsCRP in the studied groups. CRP showed a better specificity and positive predictive value than PTX3 in both group 2a and group 2b. PTX3 shows a better sensitivity and negative predictive value than hsCRP in non-dialytic therapy patients and a better sensitivity value than hsCRP in hemodialysis patients.

From the present work, it could be concluded that hsCRP and PTX3 complement each other to give a better specificity and sensitivity as predictors of inflammation in chronic kidney disease patients.

Recommendation

Study of PTX3 and hsCRP on a large number of chronic kidney disease patients with positive cardiovascular disease is recommended.

Conflict of Interest

There is no conflict of interest in this manuscript.

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