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Study of The Relation Between Plasma Pentraxin-3 Level and Diabetic Nephropathy in Type 2 Diabetic Patients

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Abstract

The aims of this study are to evaluate the changes in pentraxin-3 level in different stages of diabetic nephropathy & its relation to eGFR and albuminuria and to shed light on whether pentraxin-3 level can be considered as novel marker for early detection of diabetic nephropathy. This study was performed on 80 diabetic patients who attended endocrinology department at banha university hospital. Those diabetic patients were age and sex matched with healthy volunteers serving as control group .They were classified into 2 groups : Group 1 included 35 patients with diabetic nephropathy. Group 2 included 30 patients without nephropathy. control subjects were 15 included in Group 3 . PTX-3 level was highly significant in patients with diabetic nephropathy group compared to diabetic patients without nephropathy & control With p value <0.001. PTX-3 is significantly high in patients with albuminuria with p value <0.05 with a significant positive correlation between PTX-3 and albumin ceratinine ratio [ACR] in diabetic nephropathy group [pvalue= <.05 r= .374. Pentraxin-3 level can be considered as a novel marker of diabetic nephropathy. As pentraxin-3 is associated with diabetic nephropathy with p value <.001 . with positive association with proteinuria [pvalue = <.05 , r = .374] &\ or eGFR . [pvalue = <.001, r = -.977].

Keywords: Pentraxin-3, Diabetic nephropathy, Type 2 Diabetes.

1.Introduction

Type 2 diabetes is a major social and epidemiological problem. Today, 415 million people worldwide have diabetes and by the year 2040 this number will rise to 642 million . [30]. Diabetic nephropathy , as one of diabetic complications , is one of the leading causes of end stage renal disease. [11]. Many factors other than traditional ones, namely immunological & inflammatory mechanisms, genetic and environmental factors play role in the pathogenesis of diabetic nephropathy.[5]. Chronic low-grade inflammation resulting from activation of innate immune system has been proven to play a significant role in the pathogenesis of diabetic nephropathy and other micro vascular complications of diabetes [34]. One of the markers of this inflammatory process is Pentraxin-3 [PTX-3]. PTX-3 is a member of long pentraxins, and is synthesized by many types of cells including endothelial cells **[27].** It has properties similar to antibodies including opsonization and complement activation., and thought to be a direct marker of disease activity as it is related to endothelial dysfunction as it is synthesized directly at the site of inflammation. [33]. several clinical investigations have showed that plasma PTX-3 levels are inversely associated with e GFR, but positively associated with levels of albuminuria / proteinuria in patients with diabetic nephropathy. Hence, PTX-3 may be implicated in the development of diabetic nephropathy. [44], [16],[49]

2. Material and methods

This study was performed on 80 diabetic patients who attended endocrinology department at banha university hospital. Those diabetic patients were age and sex matched with healthy volunteers serving as control group .They were classified into 2 groups : Group 1 included 35 patients with diabetic nephropathy .Group 2 included 30 patients without nephropathy. Group 3 included 15 control subjects. Diabetic nephropathy is defined according to KADIGO as a clinical syndrome character-ized by the following : Persistent albuminuria that is confirmed on at least 2 occasions 3-6 months apart. Progressive decline in the glomerular filtration rate [GFR]. All participant were subjected to thorough history and clinical examination with special stress on duration of diabetes, the medications used by the patients, different Complications of diabetes. Anthropometric measures:weight, height, body mass index [BMI], waist circumference and Blood pressure measured using sphyngomano-meter.

1.1Biochemical methods

Venous blood samples were obtained after 12 h of fasting. Serum and plasma samples were kept at -80 C until the time of analysis for measurement of AST, ALT , S. albumin, TSH ,CBC using cell counter sysmex Europe Gmbh , Bornbarch 1, 22848, Germany, FBS was taken and measured by glucose oxidase enzymatic colorimetric method [21]. HbA1c measured by ion exchange resin method [32]. Lipid profile including Total cholesterol was measured by enzymatic colorimetric method [13]. Triglycerides was measured by enzymatic colorimetric metho [28].

HDL-c was measured by enzymatic reagen. [4]. LDL-c was calculated according to "friedwald's equation" LDL-c =total cholesterol- [HDL-c + TG/5], provided that TG is <400mg/dl [19]. Estimated GFR will be calculated according to [CKD-EPI] formula ''Chronic Kidney Disease Epidemiology Collaboration'' [25] 24-hour urine albumin execretion rate collection was performed three times, and the average of UAER was taken . ***[28]*** Plasma PTX3 level was measured by using a commercial quantitative sandwich enzyme-linked immunosorbent assays[ELISA] and kits were supplied from bioassay technology[Quantikine Human PTX-3/TSG-14 Immunoassay DPTX 30,R&D systems Inc., Minneapolis, USA [30].

Serum aliquot was stored at less than -20C until assayed for plasma PTX-3. The plasma PTX-3 level was estimated using the quantitative sandwich enzyme immunoassay technique .A streptavidin coated plate is incubated with a biotinylated monoclonal antibody specific for PTX-3. The plates are then washed and pretreated standards and samples are added to the wells. Any PTX-3 present is bound by the immobilized biotinylated antibody. An enzyme-linked conjugate specific for PTX-3 is added to the wells, and after another wash to remove any unbound conjugate, a substrate solution is added to the wells and color develops in proportion to the amount of PTX3 bound. The color development stops and the intensity of the color is measured [33].

The results of plasma PTX-3 are available in the form of standard curves that were generated for each set of samples assayed and the results were expressed in ng/ml. For PTX-3, intra-assay and interassay coefficients of variation ranged from 3.8 to 4.4% and from 4.1 to 6.1%, respectively [minimum detectable concentration: 0.025 ng/ml].

The study was approved by the local ethical committee. Informed consent form was obtained from all participants.

Statistical Analysis

The collected data were tabulated and analyzed using the Statistical Package for Social Science [SPSS 20.0]. Categorical data were expressed as number and percentage; Continuous variables were expressed as mean and standard deviation and range . Suitable tests of significance were calculated. Comparison between 2 groups was done using the student t –test. while Comparison between more than 2 groups was done using ANOVA [F] test or Kruskal Wallis [K.W] test when it was suitable , and post HOC analysis . Correlation analysis to determine the association between PNTX3 and other independent variables was done, using Pearson correlation coefficient [r] and spearman correlation coefficient [rho].The accepted level of significance in this work was 0.05[p≤ 0.05].

3. Results

The following results are reported in our results

1- PTX-3 was significantly high in diabetic patient compared to control With p value <.05 table (1).
2- PTX-3 level was highly significant in patients with diabetic nephropathy group compared to control & diabetic patients without nephropathy With p value <0.001 table (1), Fig (1)
3- mean plasma PTX-3 level increase with progression of cCkD as decline of eGFR. There is significant difference between PTX-3 level and different stages of nephropathy with p value <.001table (2), Fig (2).
4- - PTX-3 is significantly high in patients with A2 compared to A1with p value <0.05 , in A3 compared to A1with p value <.001 & in A3 compared to A2 with p value <0.05 as shown in table . A significant positive correlation between PTX-3 and albumin ceratinine ratio [ACR] in diabetic nephropathy group [pvalue= <.05 r= .374] Table (3), Fig (3).
5- -PTX-3 is significantly high in patients with retinopathy or neuropathy, with p value <.05, <.01 respectively in both diabetic and diabetic nephropathy group.
6- As assessment of different risk factors for CKD in diabetic patients with or without nephropathy , PTX-3 is significantly high in diabetic patients with or with out nephropathy patients with HbA1c > 7 with p value <.001 . Also, PTX-3 level was correlated positively with HbA1c in diabetic patients with or with out nephropathy [pvalue=<.05, r= . 340] & [p value= <.05 r= -.395] table [4] , Fig (4-6).
7- PTX-3 is significantly low with BMI more than 30 with p value <.001 & W.C more than 80 in female with p value <.01 but no significant difference in male with p value >.05] and diabetic with nephropathy group,[PTX-3 is significantly low with BMI more than 30 with p value <.001 & W.C more than 94 in male with p value <.01 but no significant difference in female with p value >.05] , Fig (5-7).
8- PTX-3 was highly significant in hypertensive than normotensive patients , in both diabetic and diabetic nephropathy group with p value <.01.
9- PTX-3 is statisticaly high with LDL more than 100 with p value <.01 in diabetic patients with or with out nephropathy .There was a negative correlation between PTX-3 and triglycerides in diabetic nephropathy group [p value=<.01, r=.-469] .A positive correlation between total cholesterol and PTX-3 in diabetic nephropathy

[pvalue= <.01, Rho=.469] . While in diabetic patient there was a positive correlation between TC and PTX-3 [p value=<.01, r= .521]Table (5).

10- There is a negative correlation between HB level and PTX-3 in DN group. [p value= <.05, r= -.347] Table (4).
11- There is no significant association between PTX-3 level and drugs used by patients

Table (1) Comparison between the mean value of PTX-3 among the studied groups.

Parameter		GroupI versus GroupII	Group I Versus Group III	GroupII versus Group III
PNTx	**t**	3.95	6.04	2.45
	P	<0.001	<0.001	<0.05

Plasma PTX-3 level is significantly high in GI and GII diabetic patients compared to control [p value <.05, <0.001 respectively] . PTX-3 is significantly high in diabetic patients with nephropathy compared to diabetic patients without nephropathy [p value <0.001].

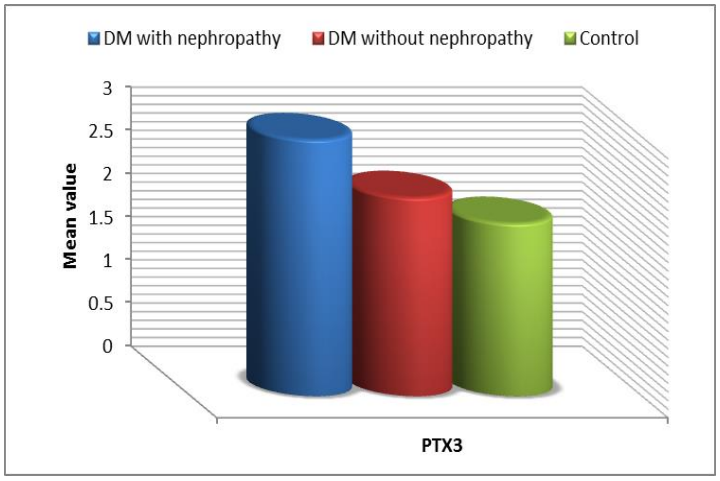

Fig (1) This figure shows that Plasma PTX-3 level is significantly high in diabetic patients with nephropathy compared to diabetic patients without nephropathy. [p value <0.001]. and to control .

Table (2) Comparison between the mean value of PTX-3 among the different stages of nephropathy [n=35].

Stage	PTX3 [n=35] Mean [$\bar{X}$] ± SD	F-test	p
1 [n= 6]	2.00 ±.000	24.50	<.001**
2 [n= 14]	3.00 ±.555		
3 [n= 7]	3.71 ±.488		
4 [n= 4]	4.00 ±.000		
5 [n= 4]	4.20 ± .000		

This table shows that mean plasma PTX-3 level increase with progression of ckD. There is significant difference between PTX-3 level and different stages of nephropathy with p value <.001 with pentraxin level increased with decline of eGFR

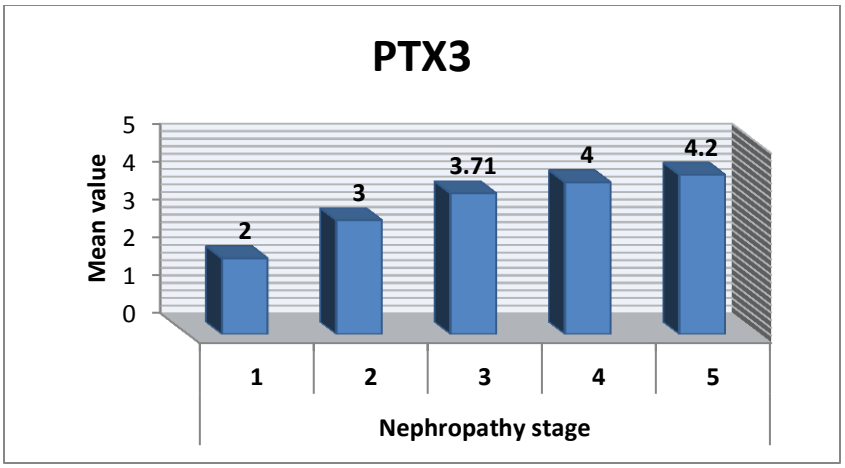

Fig (2) This figure shows that mean plasma PTX-3 level increase with progression of CkD with PTX-3 level increased with decline of eGFR.

Table (3) Comparison between the mean value of PTX-3 regarding ACR among patients with DM nephropathy [n=35].

Parameter		ACR I versus ACR II	ACR I Versus ACR III	ACR II versus ACR III
PTX-3 [n=35]	**t**	2.37	6.54	2.03
	P	<0.05	<.001	<0.05

PTX-3 is significantly high in patients with A2 compared topatients with A1with p value <0.05 , in patients with A3 compared to patients with A1with p value <.001 & in patients with A2 compared to patients with A3 with p value <0.05

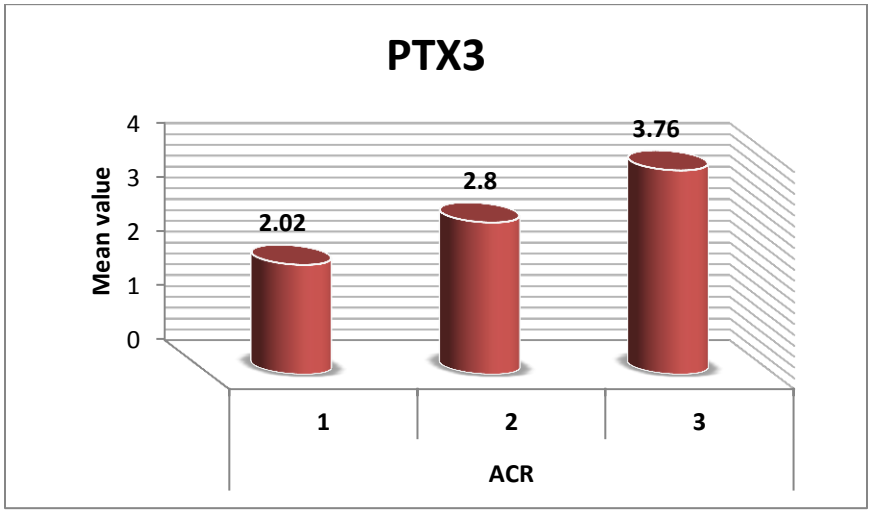

Fig (3) This figure shows that mean plasma PTX-3 level increase with progression of albuminra as PTX-3 is significantly high in patients with A2 compared to patients with A1with p value <0.05 , in patients with A3 compared to patients with A1with p value <.001& in patients with A2 compared to patients with A3 with p value <0.05

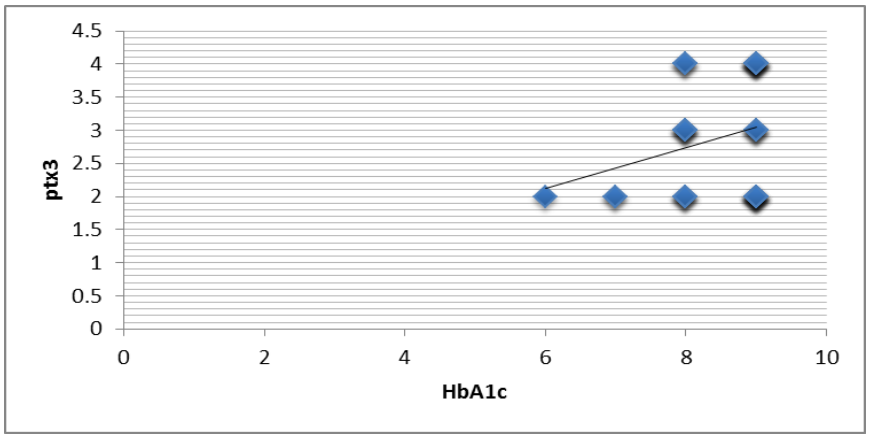

Fig (4) This figure shows that there is statistically significant positive correlation between PTX-3 level HbA1c [p value= <.05 r= -.395]

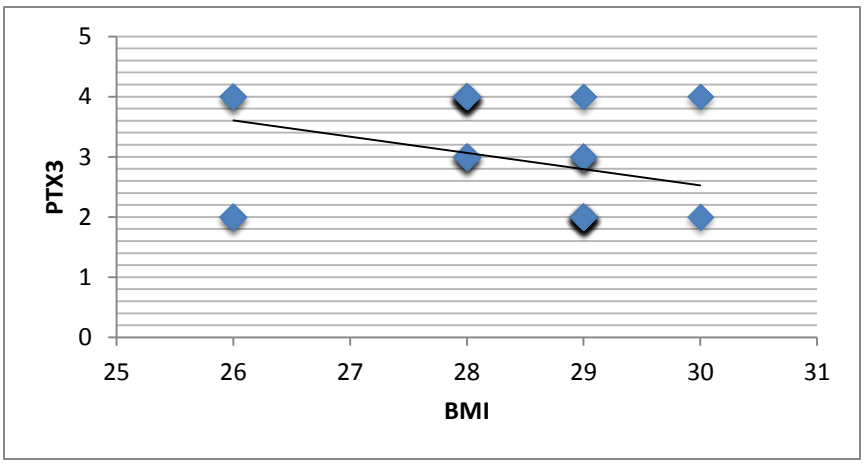

Fig (5) This figure shows that there is statistically significant negative correlation between PTX-3 level and BMI, [pvalue= <.05, r=-.-.381]

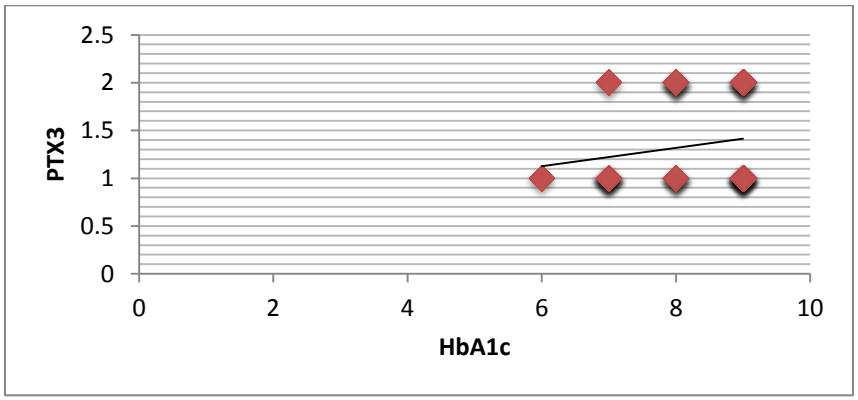

Fig (6) There is statistically significant positive correlation between PTX-3 le vel and HbA1c [pvalue=<.05, r= . 340]

Table (4) Correlation coefficient between PTX-3 and other parameters among DM patients with nephropathy [n=35].

PTX3 [n=30] parameter	r	p
age	.206	>.05
durationDM	.437	<.05
durationHTN	.094	>.05
HbA1c	. 340	<.05
Systolic bl.p	.280	>.05
Diastolic bl.p	.322	>.05
BMI	-.579	<.01
W.C	-.453	<.05
Tc	. 521	<.01
TG	-.311	>.05
HDL	-.028	>.05
LDL	-.186	>.05
eGFR	-.203	>.05
Hb	.110	>.05

There is statistically significant positive correlation between PTX-3 level and duration of DM [p value= <.05, r= .437], HbA1c [pvalue=<.05, r= . 340] , Tc [pvalue=<.01, r= .521] . There is statistically significant negative correlation between PTX-3 level and BMI [p value= <.01 ,r=-.579], W.C [p value=<.05, r=-.453] , TG [p value= <.001, r= -.628]

Table (5) Correlation coefficient between PTX-3 and other parameters among diabetics without nephropathy [n=30].

PTX3 [n=35] parameter	r	p
age	.197	>.05
Duration DM	Rho=.653	<.001
HbA1c	.395	<.05
Duration HTN	Rho=.612	<.001
Systolic Blp	.169	>.05
Diastolic Bl p	.234	>.05
BMI	-.381	<.05
W.C	-.603	<.001
Tc	.469	<.01
TG	-.469	<.01
HDL	.103	>.05
LDL	.278	>.05
eGFR	-.977	<.001
ACR	.374	<.05
Hb	-.347	<.05

There is statistically significant positive correlation between PTX-3 level and duration of DM [pvalue= <.001, Rho=.653] , HbA1c [p value= <.05 r= -.395] ,duration of HTN [pvalue= <.001, Rho=.612] , ACR pvalue= [<.05 r= .374] , Tc [pvalue= <.01, Rho=.469] . There is statistically significant negative correlation between PTX-3 level and BMI, [p value <.05]

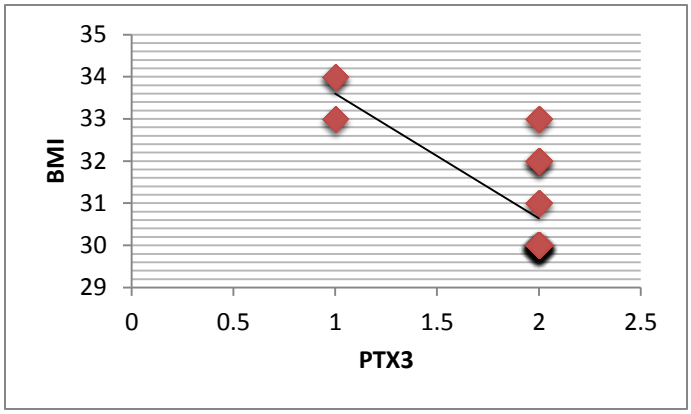

Fig (7) There is statistically significant negative correlation between PTX-3 level and BMI [pvalue= <.01 ,r=-.579]

4. Discussion

Nephropathy is a common micro vascular complication among patients `with type 2 diabetes mellitus and is a major cause of kidney failure. Detection of diabetic nephropathy during its initial stages provides the opportunity for early therapeutic interventions to prevent or delay the onset of complications and improve outcomes. [6]. Micro inflammation is a common pathway for the progression of diabetic nephropathy. In recent years, many researchers have been convinced that the inflammatory pathways play central roles in the progression of diabetic nephropathy, and the identification of new inflammatory molecules may provide early detection and link to the development of new therapeutic strategies [48].

One of these inflammatory maker is Pentraxin-3 [PTX-3] which is structurally related to other proteins of the pentraxin family , it is expressed in vascular endothelial cells and macrophages. Thereby, its levels may reflect more directly the inflammatory status of the vasculature [27]. The aim of this study is to evaluate the changes in pentraxin-3 level in diabetic nephropathy and its relation to proteinuria &or e GFR and to shed light on whether PTX-3 plasma level can be considered as a novel marker of diabetic nephropathy. The relation between diabetes and PTX -3 is complex whether they share a common pathogenic mechanism or one of them is the cause or the effect is still unknown . In our study we found that diabetes has a significant impact on the level of PTX-3 in plasma as it was significantly high in diabetic patient compared to control With p value <.05 . Elevation of pentraxin-3 in type 2 diabetes can be explained by low-grade inflammation caused by insulin resistance, as insulin resistance correlated with markers of inflammation, such as CRP and PTX-3 [41]. This was consistent with [18] who reported that hyperglycemia is associated with increased oxidative stress that is considered an important regulative factor on PTX-3. On the other hand, other studies showed that the median PTX-3 concentration did not differ significantly between patients with and without diabetes [46],[44], [40] . Whether plasma PTX-3 protect against local inflammation or exacerbate the expansion of tissue damage, i.e , whether it can be considered as a cause or effect of inflammation is amatter of debate . PTX-3 was thought to have a pathogenic role in inflammation mediated by insulin resistance and was considered as a better indicator of inflammation and endovascular damage in diabetic patients. [40],[43]. However, other studies declared that PTX-3 plays tissue protective and anti-inflammatory roles. [33]. This controversy may be due to different levels of PTX-3 noticed in males and females in different studies or due to racial difference, different analytical methods & presence of confounding factors. we also assesed different risk factors for diabetic nephropathy and their impact on pentraxin-3 level. we found that the state of glycemic control had a significant impact on PTX-3 level, as PTX-3 was significantly highin diabetic patients withor without nephropathy who have HbA1c more than 7. Also, PTX-3 level was correlated positively with HbA1c . That was consistent with different studies that reported a significant positive correlation between PTX-3 levels and the duration of diabetes, fasting plasma glucose level, HbA1c level. [40] [45]. However, [47] reported that there was no correlation between PTX-3 and glucose, HbA1c, C-peptide, insulin and HOMA-IR. We also found that both body mass index and waist circumference had a negative impact on PTX-3 level in plasma in diabetic patients with or without nephropathy. Also, plasma PTX-3

level was negatively correlated with BMI& W.C in both diabetic patients with or without nephropathy

.There are different hypotheses to explain this relation . it was postulated that PTX-3 may have a protective role similar to adiponectin as it was found to be positively correlated with adiponectin [an adipocyte specifc plasma protein with anti atherosclerotic properties] that was inversely proportional to obesity and T2DM in different populations compared to that in healthy control subjects [26] . another explanation iwas that PTX-3 may be antagonistically participated in the development of obesity or metabolic syndrome, and despite the lower PTX-3 protein levels in plasma, the PTX-3 gene expression is upregulated in visceral adipose tissue depots in obesity and in cultured adipocytes by some proinflammatory cytokines [35]. Also, the relation between HDL and PTX-3 level can be another cause ,as lower levels of HDL cholesterol might lower plasma PTX-3 concentrations in obese individuals or in those with metabolic syndrome as shown in a study by [35] that expression of the PTX-3 gene is stimulated by HDL-C in cultured human umbilical vein. However, the cause of the decreased PTX-3 level in obesity or metabolic syndrome cannot be explained simply by a relationship between PTX-3 and HDL-C, because they could not identify a positive association between them. Our results were consistent with a study by [50] showing an inverse relation between serum levels of PTX-3 and BMI & W.C, Detailed data from DXA and magnetic resonance imaging suggests that fat mass, specifically visceral fat, largely accounts for this association. They confirmed these results using longitudinal data over a 5 year period and during a 6week dietary intervention, where weight loss was associated with an increase in serum PTX-3 levels. Different studies showed an inverse correlation between PTX-3 and BMI suggesting that PTX-3 may play a role in obesity and metabolic syndrome. [37][& 38]. However, a study by [2] suggested that obese individuals had elevated plasma PTX-3 protein levels and an increased visceral adipose tissue PTX-3 expression that associated with a cardiovascular risk profile, including low HDL-cholesterol and high fibrinogen. These discrepant results may be explained by limited sample size and the inclusion of disease specific populations, or due to differences in prevalence of obesity in the different study samples. Also, Our result showed that dyslipidemia had a significant impact on PTX-3 level in diabetic patients with and without nephropathy with LDL ≥100. A positive correlation was found between total cholesterol and PTX-3 in diabetic nephropathy . While there was a positive correlation between TC and PTX-3 in diabetic patient , there was a negative correlation between PTX-3 and triglycerides inpatients with diabetic nephropathy . This effect of dyslipidemia on PTX-3 level may be due to the endothelial dysfunction caused by hyper-cholesterolemia, as reported by a study that showed that a reduction in plasma cholesterol levels [after using a lipid lowering agent] could improve the vascular function in patients with type 2 diabetes. [31].

More over, a potential link between the level of LDL and the expression of genes involved in inflammation oxidative stress pathways, i.e., p66[ShcA] and PTX-3 was found , thus contributing to further understand the mechanism through which LDL may mediate the pathogenesis of inflammation and oxidative-stress associated diseases such as atherosclerosis. They found that the patients with high levels of circulating LDL show a significant increase of PTX-3 mRNA levels in adipose tissue and in WBC cells. Additionally, a multiple regression analysis indicated that the only variable significantly affecting PTX-3 mRNA expression is represented by the circulating level of LDL. **[8].** Also, a study on Japanese population showed that plasma pentraxin level was inversely correlated with triglycerides and BMI. **[37],[35].** However, different studies showed that there was no association between lipid parameters [cholesterol, triglycerides, and HDL cholesterol] and PTX-3 level . [46] ,[39]. Our results showed that elevated blood pressure had also a positive impact on PTX-3 level. As it was highly significant in hypertensive patients than normotensive patients , in diabetic patients with or without nephropathy. PTX-3 was found to play a direct role in vascular function and blood pressure homeostasis, suggesting that P-selectin, MMP-1, and PTX-3 may be novel biomarkers that can predict the start of vascular dysfunction in hypertensive patients [9]. This was consistent with a study by [39] that revealed that PTX-3 levels were found to be higher in newly diagnosed hypertensive patients than in healthy individuals & these increases in PTX-3 correlated with increasing in systolic and diastolic blood pressure. However, a study performed in 2009 stated that there was no detected relation between CRP and PTX-3 levels in cardiovascular diseases. This study also revealed no significant relation between CRP and PTX-3 levels in the hypertensive group. [22]. In our study we found that diabetic nephropathy had a significant impact on PTX-3 level as it was highly significant in [DN] group compared to control & diabetic patients without nephropathy With p value <0.001.The mechanisms underlying the inverse association between PTX-3 levels and kidney function remain unclear; however, several potential mechanisms may explain how high PTX-3 levels

mirror impaired kidney function. [42]. First, PTX-3 is an important factor in the regulation of inflammation , as it activates and regulates the complement cascade and because PTX-3 is produced and stored in the vasculature, rapid release is possible in response to stimulation by cytokines. Therefore, PTX-3 is thought to have a protective counter-regulatory role in the acute-phase reaction [14] . Another possible explanation is that PTX-3 has no protective or causal role in CKD pathology but that higher circulating PTX-3 is merely due to decreased renal clearance [42]. Our results were consistent with several studies that reported association of PTX-3 with DN. As seen in study on Turkish patients with T2DM that showed that PTX-3 was increased in early stages of renal damage in patients with diabetes, even when GFR seems to be normal With impaired flow mediated dilation [FMD] in patients with stage 1 diabetic chronic kidney disease. [44]. Also, a study on rat model injected with streptozotocin to induce DN Model, reported that PTX-3 is involved in the development of DN. However, its mechanism of action still unclear. [10]. However, a study by [38] , analyzed plasma PTX-3 levels in Malay subjects with NGT and T2DM with and without DN provided evidence that decreased plasma Ptx-3 levels were associated with type 2 diabetes and diabetic nephropathy. This controversy may be caused by The racial differences of plasma PTX-3 level . [15], The ages of T2 diabetic patients were different [44] , [38] & presence of different causes of CKD as diabetes and high blood pressure, which are responsible for up to two-thirds of the cases [29]. Pentraxin as a marker of endothelial function was found to be associated with albuminuria **[3] , [12].** In our study , PTX-3 was significantly associated with albuminuria with a significant positive correlation between PTX-3 and albumin ceratinine ratio [ACR]in diabetic nephropathy group. A study on Egyptian patients reported that type 2 diabetic patients with microalbuminuria and a normal glomerular filtration rate had significantly higher PTX-3 concentrations and significantly lower FMD compared with the control group and the group of diabetic patients with a normal urinary albumin excretion. [17]. Also, [44] found a relationship between PTX-3 level, proteinuria and endothelial dysfunction in patients with stage 1 DN and patients with stage-5 CKD due to various etiologies. However other studies did not agree with that and showed no association between PTX-3 plasma level and the degree of proteinuria . [38],[36]. This contoversy can be due to different methods used to assess proteinuria. Also, some studies were on highly selected type 2 diabetic patients and may not be representative of most patients with type 2 diabetes .In our study we found that mean plasma PTX-3 level increase with progression of cCkD as decline of eGFR. There is significant difference between PTX-3 level and different stages of nephropathy with p value <.001 That was consistent with a study by [36] that found that levels of PTX-3, IL-1 and TNF-α increased as the stage of DNP progresses while hsCRP level did not change significantly. A North American cross-sectional study found that high PTX-3 levels were associated with lower GFR even after adjustment for demographic characteristics, comorbidities and IL-6 level, but this association was strongest amongst Blacks and non significant amongst Whites [15]. We also noticed that plasma PTX-3 was closely associated with diabetic retinopathy and neuropathy and this can be explained as pentraxin is a marker of endothelial dysfunction and has a protective role as it can be used as anti angiogenic molecule as mentioned in a study by Zhou & Hu ,2016 which suggested that the use of PTX-3 could be used as an anti-angiogenic molecule because PTX-3 interacts specifically with factor reducing the proliferative diabetic retinopathy thus ameliorating diabetic retinopathy condition. our results were consistent with a study by [52] who suggested that plasma PTX-3 is closely associated with diabetic retinopathy development and progression, and may be a better predictor for diabetic retinopathy development than hsCRP in diabetic patients. Also, different studies demonstrated that PTX-3 may contribute to the onset of nociceptive pain in diabetic patients. And it may be due to tissue damage It was found that PTX-3 levels were significantly higher in diabetic polyneuropathy patients. [20] [24]. Others showed no significant or inverse relation between CRP as inflammatory marker and diabetic retinopathy. [50],[52] . In our study we found that there is no significant association between PTX-3 level and drugs used by patients. This was consistent with a study by [7] which was performed on patients with type 2 diabetes treated with insulin for 6 months, it reported that hsCRP was positively associated with insulin doses. No such association was found for pentraxin- 3, a more specifc marker of vascular inflammation, and for nitrotyrosine as a marker of oxidative stress. A study by [47] reported that the intake of common medication [ACEI, calcium channel blockers, beta blockers, and statins] or smoking habits did not affect PTX-3 levels. However, another study reported that valsartan and amlodipine improved FMD and normalized PTX-3 levels and proteinuria in type 2 diabetic hypertensive patients with proteinuria, and that the improvement in FMD was independently associated with PTX-3 normalization. [53].

5.Limitations Of Our Study

1- This is across sectional study that can't asses the actual role of pentraxin in diabetic nephrothy.

2- we depend on albuminuria as amarker of endothelial dysfunction which is alate marker compared to other methods as VWF assay or brachial flow mediated dilation.

6. Conclusions

Pentraxin-3 can be considered as a novel marker of diabetic nephropathy. As pentraxin-3 is associated with diabetic nephropathy with p value <.001 . with positive association with proteinuria [pvalue = <.05 , r = .374] &\ or eGFR . [pvalue = <.001, r = -.977].

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