Evaluation of YKL-40 in Patients with Type II Diabetes Mellitus with Increasing Levels of Albuminuria

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ABSTRACT

Background and Aim of work: *The aim of the present study is to evaluate serum YKL-40 levels in patients with type II diabetes with increasing levels of albuminuria, and to examine a possible correlation to high-sensitivity C-reactive protein (hsCRP) and insulin resistance in these patients.* ***Methods:*** *The study comprised 125 patients with type II diabetes attending Diabetes& Endocrinology Unit in Mansoura Specialized Medical Hospital. They were divided into 3 groups: 39 patients had normoalbuminuria (urinary albumin excretion rate < 30 mg/24 h), 46 patients had persistent microalbuminuria (urinary albumin excretion rate 30–300 mg/24 h), and 40 patients had persistent macroalbuminuria/diabetic nephropathy (urinary albumin excretion rate > 300 mg/24 h). The control group included 35 healthy individuals with matched age and sex. Serum YKL-40 was measured by sandwich enzyme immunoassay and serum hsCRP was measured by particle enhanced immunonephelometry. Insulin resistance was assessed using Homeostasis Model Assessment index for Insulin Resistance (HOMA-IR).* ***Results:*** *Mean serum YKL-40 level was 38.48ng/ml, 75.33ng/ml, 116.87ng/ml and 146.43ng/ml in control, normo- , micro- and macroalbuminuria groups respectively. Serum YKL-40 levels were significantly elevated in the three diabetic groups versus control group ($P < 0.001$ for each group). Also, YKL 40 was correlated with hsCRP and HOMA-IR ($r = 0.746$, $P < 0.001$ & $r = 0.792$, $P < 0.001$, respectively) in the total group of participants. ROC curve analysis showed that YKL-40 is a good marker to discriminate between patients with and without albuminuria with sensitivity 93% and specificity of 88%.* ***Conclusion:*** *It could be concluded that YKL-40, is a marker of inflammation and endothelial dysfunction. It is elevated in patients with type II diabetes with marked elevation in patients with macroalbuminuria/ nephropathy. These results suggest a role for YKL-40 in the gradually progressing vascular complications in patients with diabetes, with YKL-40 being a possible early and good marker of renal affection. It seems to be useful for screening because it is detectable in early stages and subclinical diseases.*

Key words: *YKL-40, type II diabetes, diabetic nephropathy, insulin resistance, hsCRP*

INTRODUCTION

Diabetes is a major health problem in the world, the micro- and macrovascular complications remain a constant challenge to the quality of life as well as increasing morbidity and mortality rate [(1)]. Persistent microalbuminuria is an established predictor of diabetic nephropathy leading to progressive renal insufficiency and end-stage renal disease and is associated with an increased risk of cardiovascular disease in patients with both type I and type II diabetes [(2-4)].

Increasing urinary albumin excretion rate reflects vascular damage in the kidneys as part of systemic endothelial dysfunction [(5)]. Endothelial dysfunction is the initial step in atherogenesis, which is largely responsible for the development of ischemic heart disease and thrombotic strokes [(6)].

Subclinical systemic inflammation is involved in the pathogenesis of all stages of atherosclerosis [(7)]. Low grade elevation of acute phase reactants, proinflammatory cytokines and cell adhesion molecules were shown to be associated with future development of myocardial infarction, stroke and peripheral vascular disease with cardiovascular mortality [(8)]. Several studies suggest that activation of innate immune system likely to be at least one of common antecedents of both atherosclerosis and type II diabetes. YKL-40 was reported to be a marker of inflammation and endothelial dysfunction [(9)]. It is produced locally at sites of inflammation, [(10)] unlikely to C-reactive protein produced by liver in response to IL-6 [(11)].

YKL-40, a phylogenetically highly conserved heparin- and chitin-binding lectin without chitinase activity, is a member of the ‘‘mammalian chitinase-like proteins’’ [(7, 12-14)]. The gene for human YKL-40 is located on chromosome 1q32.1, has a size of 7948 b.p and contains 10 exons [(15)]**.** The crystal structure of human YKL-40 protein has been described [(16, 17)].The protein has several names: YKL-40 [(18)], human cartilage glycoprotein-39 (HC gp39)[(7)], 38-kDa heparin-binding glycoprotein (Gp38k) [(13)],and chitinase-3-like protein 1 (CHI3L1) [(15)].

YKL-40 is secreted by a variety of human cells including activated neutrophils, [(19)] chondrocytes, synovial cells and osteoblasts but greatest hypothesis that it is secreted from vascular smooth muscle cells (VSMCs) and macrophages [(20, 8)]. Atherosclerotic plaque macrophages express YKL-40, particularly macrophages that have infiltrated deeper into the lesion and the highest YKL-40 mRNA expression is found in macrophages in the early atherosclerotic lesion [(21)].

The full biological functions of YKL-40 are still unknown [(22)]. It is a growth factor for several cell types and has an established role in extracellular matrix remodeling and angiogenesis [(9)]. A substantial body of evidence indicates that YKL-40 participates in processes during the early stages of atherosclerosis, and it seems to be of pathogenic importance in the low-grade inflammation that precedes the development of cardiovascular disease[(9,13)].

The participation of YKL-40 in inflammatory states and vascular processes implies that YKL-40 may be elevated in conditions with subclinical

inflammation such as type II diabetes and insulin resistance as well as endothelial dysfunction and atherosclerosis [23].

The objective of the present study was to evaluate serum YKL-40 levels in patients with type II diabetic patients who have increasing levels of albuminuria .Also, to examine a possible correlation to hsCRP and insulin resistance.

Subjects and methods

Using a case-control design, the diabetic participants were examined at the Diabetic & Endocrinology Unit in Specialized Medical Hospital, Mansoura University, Egypt. The study comprised 125 patients with type II diabetes (66 males & 59 females) with age ranged from 40 – 68 years. On the basis of 24-h urine analysis as part of the routine care of the patients, they were divided into; 39 patients with normoalbuminuria (urinary albumin excretion rate <30 mg/24 h), 46 patients with persistent microalbuminuria (at least two of three consecutive urine samples with albumin excretion rate 30– 300 mg/24 h), and 40 patients with persistent macroalbuminuria/diabetic nephropathy (albumin excretion rate >300 mg/24 h). Diabetic retinopathy was assessed in all patients by fundus photography after pupillary dilatation and graded as nil, simplex, or proliferative. Control subjects were randomly selected from the general healthy population with matching age and sex. They had no signs or clinical symptoms of cancer, liver, metabolic, endocrinal, cardiovascular, or other systemic diseases. The study was approved by the local ethics committee. Prior to participation all patients and controls gave their informed written consent.

Biochemical analysis

Urinary albumin concentration was measured by Siemens Healthcare Diagnostics Inc., USA, from 24-h urine sample.

Eight ml venous blood sample was drawn, in the morning after overnight fasting (10-12 h), 7 ml on a plain tube and serum was separated after centrifugation at 2500 rpm × 10minutes, then stored frozen at -80^{0}C until analysis. One ml from the sample was placed on EDTA tube for HbA_{1c} determination (COBAS, INTEGRA, Roche Diagnostics, USA). Serum glucose and lipid profile (total cholesterol, HDL-cholesterol & triglyceride) were measured by Siemens Healthcare Diagnostics Inc., USA. Using Dimension RXL Max clinical chemistry system (Dade Behring USA). LDL- cholesterol concentration was calculated by the **Friedewald** equation, 1972 [24].

Hormonal assay (insulin & C-peptide) was measured by electrochemiluminescence immunoassay (Cobas, Roche Diagnostics, USA). Insulin resistance was assessed using HOMA model (Homeostasis Model Assessment index) for insulin resistance = Fasting Insulin (μU/ml) x Fasting glucose (mg/dl) x 0.055 / 22.5 [25].

Serum creatinine was measured by Siemens Healthcare Diagnostics Inc., USA. Glomerular filtration rate was estimated (eGFR) using the four variable Modification of Diet in Renal Disease GFR formulas (age, sex, race, and serum creatinine) as follow: eGFR = 186 x (serum creatinine$^{-1.154}$) x (age$^{-0.203}$) x (0.742 if female) [26].

Serum YKL-40 was analyzed with a commercial assay kit ((METRA, YKL-40 EIA kit, QUIDEL, USA).

Cardiophase hsCRP was estimated using an in vitro diagnostic reagent for the quantitative determination of C-reactive protein in human serum by means of particle enhanced immunonephelometry using BN system (Dade Behring, USA).

Statistics:

The statistical analysis was performed by the SPSS 15.0 package (Statistical Package for the Social Sciences, SPSS Inc., Chicago, Illinois, USA). Unpaired student t-test was used to compare between two groups. Also, one-way ANOVA (F-test) was used to compare between more than two groups. Correlations among variables were done by spearman's correlation coefficient and linear regression analysis. ROC curve was drawn to test sensitivity and specificity. A two-sided p value < 0.05 was considered significant. Qualitative data are presented as number and percent. Quantitative data are presented as mean ± standard deviation or median (minimum – maximum) where appropriate.

RESULTS

Clinical and biochemical data for the control group and the diabetic patients differentiated according to level of albuminuria are shown in (Tables 1&2). YKL-40 levels according to level of albuminuria are illustrated in (Fig.1). Mean YKL-40 levels were highly significantly different among all groups ($P < 0.001$), with increasing YKL-40 levels with the increase levels of albuminuria. Moreover, pairwise comparisons showed a highly significant difference between each two groups ($P < 0.001$).

Highly significant lower eGFR was found in the micro- and macroalbuminuria groups ($P < 0.001$, for each group) but no significant difference in normoalbuminuria group ($P = 0.456$) versus control group. Other pairwise comparisons showed a highly significant difference ($P < 0.001$).

There was highly significant increase of serum hsCRP in all diabetic groups versus control group ($P < 0.001$, for each group), while there was no significant difference between micro- and macroalbuminuria groups ($P = 0.058$). Also, for HbA_{1c} there was highly significant increase in each diabetic group versus control group ($P < 0.001$). No significant difference between micro- and macroalbuminuria groups was found ($P = 0.469$), there was a highly significant increase in both groups versus normoalbuminuria group ($P < 0.001$).

For insulin resistance expressed as HOMA model there was highly significant increase in all diabetic groups versus control group ($P < 0.001$ for each group). While, a significant difference between micro- and macroalbuminuria groups was found ($P = 0.006$), there was highly significant increase in both groups versus normoalbuminuria group ($P < 0.001$).

There was highly significant increase of serum TG, total-C and LDL-C in each diabetic group versus control group ($P < 0.001$), but highly

significant decrease of serum HDL-C in the three groups versus control group ($P < 0.001$).

Regarding diabetic retinopathy, there was no significant difference of YKL-40 levels between the different grades of retinopathy within each diabetic group (P = 0.053, 0.391& 0.859 within normo-, micro- & macroalbuminuria groups respectively) (Table 3).

Pearson's correlation between YKL 40 levels and different parameters showed correlation of YKL 40 with hsCRP and HOMA-IR (r = 0.746, $P < 0.001$ & r = 0.792, $P <$ 0.001, respectively) in the total group of participants. But, this correlation was not significant in any of the different subgroups. Significant correlations of YKL-40 were also found with duration of diabetes, Hb A_{1C}, eGFR (negative correlation), serum creatinine, TG, total-C, HDL-C (negative correlation), LDL-C and urinary albumin in the total group of participants (Table 4).

The changes by stepwise linear regression analysis showed that, YKL-40 levels were affected by serum TG, eGFR and hsCRP (P =0.005, < 0.001& = 0.045 respectively), but not affected by HOMA-IR (P = 0.192) in the total group of participants (patients & control).

ROC curve was done to discriminate between patients with and without albuminuria, using YKL-40 as a discriminator between both groups. The results showed that, the cut off value of YKL-40 is 87.5 ng/ml (area under the curve = 0.971) with sensitivity 93% and specificity 88% (Fig. 2).

Table 1: Clinical data of the control subjects and diabetic patients.

	Control (n = 35)	**Normo-albuminuria (n = 39)**	**Micro-albuminuria (n = 46)**	**Macro-albuminuria (n = 40)**
Sex, Male (%)	19 (54.3)	19 (48.7)	23 (50)	24 (60)
Sex, Female (%)	16 (45.7)	20 (51.3)	23 (50)	16 (40)
Age (years)	49.26 ± 4.7	52.46 ± 5.55	54.65 ± 6.29	57.38 ± 5.83
Diabetes duration (years)	-	6.62 ± 2.82	10.43 ± 2.75	14.68 ± 4.13
Retinopathy (%)				
None	-	7 (17.9)	5 (10.9)	4 (10)
Simplex	-	19 (48.7)	19 (41.3)	13 (32.5)
Proliferative	-	13 (33.3)	22 (47.8)	23 (57.5)

Data are mean ± SD & number (%).

Table2: Biochemical data of the control subjects and diabetic patients.

	Control (n = 35)	**Normo-albuminuria (n = 39)**	**Micro-albuminuria (n = 46)**	**Macro-albuminuria (n = 40)**	***F values***	***ANOVA P***
Urine albumin (mg/24 hour)	-	19.97 ± 5.44	117.46 ± 28.59	443.33 ± 100.90	552.051	< 0.001
YKL- 40 (ng/ml)	38.48 ± 10.0	75.33 ± 16.47	116.87 ± 27.06	146.43 ± 27.74	172.270	< 0.001
Glucose (mg/dl)	89.29 ± 10.5	147.64 ± 21.18	222.30 ± 30.10	273.55 ± 41.94	300.220	< 0.001
C.peptide (pM)	3.54 ± 0.54	2.20 ± 0.48	2.80 ± 0.55	3.56 ± 0.57	57.918	< 0.001
Insulin (pM)	46.85 ± 10.72	28.36 ± 6.17	34.98 ± 9.29	63.35 ± 7.55	128.896	< 0.001
HOMA-IR	1.31 ± 0.55	3.42 ± 0.48	5.98 ± 1.62	6.73 ± 0.72	231.435	< 0.001
Total-C(mg/dl)	159.86 ± 16.42	227.77 ± 42.61	213.72 ± 22.59	260.95 ± 51.89	49.587	< 0.001
HDL-C (mg/dl)	55.83 ± 6.86	45.59 ± 7.64	42.20 ± 6.18	32.98 ± 3.95	84.623	< 0.001
LDL-C (mg/dl)	86.2 ± 16.19	114.00 ± 22.40	123.30 ± 8.79	139.03 ± 15.60	69.567	< 0.001
TG (mg/dl)	111.97 ± 19.37	183.05 ± 20.84	210.50 ± 35.59	213.28 ± 31.21	103.794	< 0.001
Creatinine (mg/dl)	0.77 ± 0.18	1.04 ± 0.26	1.63 ± 0.36	1.81 ± 0.32	106.456	< 0.001
eGFR (ml/min per 1.73 m^2)	81.86 ± 15.15	79.90 ± 5.81	62.65 ± 10.33	47.83 ± 7.65	95.736	< 0.001
hsCRP (ng/ml)	1.91 ± 0.8	3.31 ± 0.67	5.67 ± 1.24	6.19 ± 1.27	141.749	< 0.001
HbA1c (%)	4.5 ± 0.9	7.18 ± 0.50	7.89 ± 0.70	8.04 ± 1.04	13.932	< 0.001

Data are mean ± SD. HOMA-IR > 2.5 was interpreted as impaired insulin sensitivity or insulin resistance. Significant *p*: < 0.05

Table 3: Relation between YKL-40 levels and the grade of retinopathy within each group of the diabetic group.

	None	Simplex	Proliferative	F	*p*
Normoalbuminuria	71.6 ± 15.8	70.6 ± 17.0	84.2 ± 13.1	3.183	0.053
Microalbuminuria	108.8 ± 19.4	112.4 ± 28.0	122.6 ± 27.5	0.961	0.391
Macroalbuminuria	143.3 ± 42.8	149.9 ± 26.3	145.0 ± 27.0	1.101	0.859

Data are mean ± SD. Significant p < 0.05

Table 4: Correlation between YKL-40 and different parameters in the total group of participants (n=160)

	Correlation coefficient r	*P*
Diabetes duration	0.562	< 0.001
Urine albumin	0.672	< 0.001
HOMA-IR	0.792	< 0.001
Total-C	0.561	< 0.001
HDL-C	- 0.660	< 0.001
LDL-C	0.667	< 0.001
TG	0.693	< 0.001
Creatinine	0.723	< 0.001
eGFR	- 0.735	< 0.001
hsCRP	0.746	< 0.001
HbA1c	0.305	< 0.001

Significant *p*: < 0.01

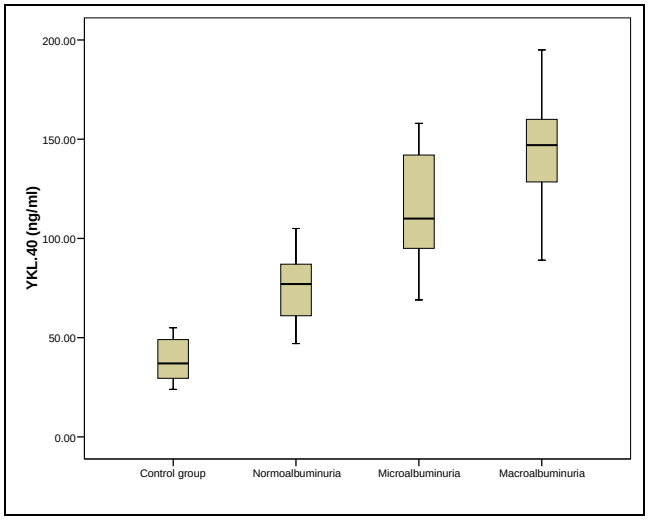

Figure 1: Median levels (minimum-maximum) of YKL-40 in the three diabetic groups compared with the control group: 37 (24-55) ng/ml in the control group, 77 (47-105) ng/ml in the normoalbuminuria group, 110 (69-158) ng/ml in the microalbuminuria group, 147 (89-195) ng/ml in the macroalbuminuria group (p < 0.001 for each group Vs control group).

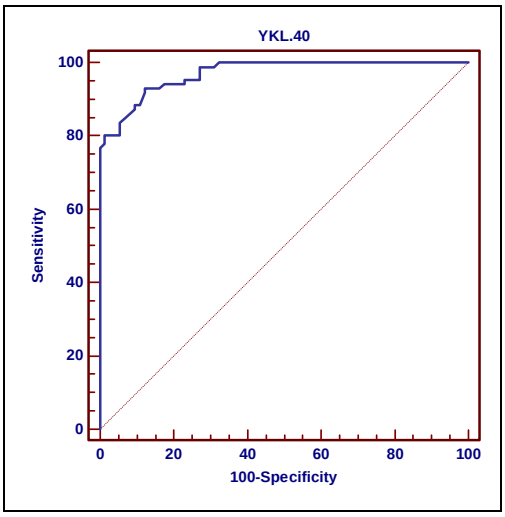

Figure 3: Roc Curve analysis to discriminate between patients with & without albuminuria using YKL-40 as a marker. The YKL-40 criterion Value is 87.5 ng/ml (area under the curve = 0.971). Ykl-40 values > 87.5 ng/ml indicate albuminuria with sensitivity 93% and specificity 88% (vice versa).

DISCUSSION

Despite improvement and intensified treatment modalities in diabetic patients, still several researches focus on more depth in the pathogenesis and complications of these patients, looking for new inflammatory markers and cytokines that enhance vascular endothelial dysfunction and its role in subclinical inflammation [(27)].

YKL-40 has been regarded as an acute phase protein, since it is secreted from a variety of cells involved in infection/inflammation. The participation of YKL-40 in inflammatory states and vascular processes implies that YKL-40 may be elevated in conditions with subclinical inflammation such as type II diabetes and insulin resistance as well as endothelial dysfunction and atherosclerosis [(23)].

The present study showed that serum YKL-40 levels were elevated in patients with type II diabetes compared to healthy controls, with increasing YKL-40 levels with the increase in the levels of albuminuria. This finding is in agreement with previous studies showing that chronic low-grade inflammation is associated with the occurrence and progression of (micro)albuminuria [(28)] and that both micro- and macroalbuminuria are accompanied by increased levels of a variety of markers of endothelial dysfunction.[(1)] Also, other studies reported that patients with type II diabetes have elevated plasma YKL-40 levels compared to healthy control subjects [(23, 29-32)].

Chronic low-grade inflammation and endothelial dysfunction seem to be closely linked, and it seems that

chronic low-grade inflammation can be both a cause and a consequence of endothelial dysfunction. Dysfunction of the vascular endothelium is considered an important factor in the pathogenesis of diabetic micro- and macroangiopathy [1, 33].

Previous studies showed that YKL-40 plays a role in endothelial dysfunction in relation to cell migration, reorganization, and tissue remodeling during atherogenesis [13, 34, 35]. YKL-40 promotes chemotaxis, cell attachment, spreading, and migration of vascular endothelial cells, suggesting that YKL-40 promotes the process of atherosclerotic plaque formation, in which VSMCs are induced to migrate through the intima in response to exogenous signals. YKL-40 also modulates vascular endothelial cell morphology by promoting the formation of branching tubules, indicating a role of YKL-40 in angiogenesis by stimulating the migration and reorganization of VSMCs [35]. Furthermore, YKL-40 is produced and secreted by monocytes during differentiation to macrophages and is also secreted by activated macrophages [9]. Therefore, YKL-40 seems to be a part of early stages of atherosclerosis and low grade inflammation that precedes the development of cardiovascular diseases[36]. Immunohistochemical analysis of different types of human tissues showed high YKL-40 expression with high cellular metabolic activity and/or proliferation as fibroblast, chondrocytes & synovial cells [37].

Other studies suggest that YKL-40 expression is an anti-inflammatory counteract of the inflammatory response mediated by tumor necrosis factor α (TNF-α) and interleukin-1 (IL-1) beside its apparent function as a growth factor. The activation of cytoplasmic signal – transduction pathways suggests that YKL-40 interacts with one or several signaling components on the plasma membrane. However, specific cell surface receptors or potential YKL-40 ligands remain to be determined [38].Several studies have investigated the role of YKL-40 in relation to cancer but the results are still conflicting. YKL-40 levels are particularly high in recurrent cancer states and highly differentiated cancers which are characterized by high vascularization and a high turnover of extracellular matrix [36].

In the present study, there is a significant decrease in eGFR only in diabetic patients with micro- and macroalbuminuria compared to healthy controls (diabetic patients with normoalbuminuria showed no difference in eGFR with healthy controls). This result is in harmony with other studies that found YKL-40 is associated with a decline in eGFR in diabetic patients [33, 39, 40].

Diabetic nephropathy is a major manifestation of microangiopathy and is graded according to the urinary albumin excretion rate. Micro- as well as macroalbuminuria are important markers for the progression of renal dysfunction and are currently recognized as predictive factors for cardiovascular adverse events [41]. The earliest clinical evidence of nephropathy is the appearance of low but abnormal levels of albumin in the urine, referred to as microalbuminuria. Once overt nephropathy occurs the

glomerular filtration rate gradually falls [42]. Decreases in GFR in patients with type II diabetes have been linked to increase in carotid intimal-medial thickness, carotid stiffness, and increases in the intra-renal arterial resistance index. This has led to the suggestion that the decline in GFR in type II diabetes is in part due to generalized increase in arteriosclerosis[39].

For HOMA –IR results, the present study showed an increase in insulin resistance in patients with type II diabetes compared to healthy controls, with more increase in patients with macroalbuminuria. Also, YKL-40 was found to be correlated with HOMA-IR. This result is in agreement with previous studies which found that subclinical inflammation was strongly related to insulin resistance (HOMA-IR) [43, 44] and that in patients with type 2 diabetes plasma YKL-40 are correlated with insulin resistance [30]. Also, **Rathcke et al.** [33] reported that HOMA-IR was approximately 3.5-fold higher in type II diabetic patients and correlated with elevated levels of YKL-40. Generally, insulin resistance can be explained by the presence of subclinical systemic inflammation in type II diabetic patients [23].

Also, the present study showed elevated levels of hsCRP in patients with type II diabetes compared to healthy controls, with more increase in macroalbuminuria group. This result is in agreement with previous studies that found hsCRP is increased in type II diabetic patients [23, 45, 46]. Subclinical systemic inflammation and abnormalities of a wide variety of systemic inflammatory markers have been reported in type II diabetes [23]. CRP is an acute phase response protein markedly increased in both inflammatory and infectious diseases and it also, plays an important role in innate immunity [46, 47] These observations suggest that low-grade inflammation, reflected by high serum hsCRP levels, plays a role in the induction of albuminuria, which can be considered as a risk factor of cardiovascular diseases [45]. Moreover, YKL-40 was found to be correlated with hsCRP. This is in accordance with previous studies that reported a positive correlation of elevated levels of serum YKL-40 with serum levels of CRP [29, 48]. However **Rathcke et al.** [33] found no correlation between hsCRP and YKL-40 in type II diabetic patients. This controversy can be explained by smaller number of diabetic patients in his study and all patients chosen in his study had no clinical or biochemical signs of diabetic complications. The perception of YKL-40 as an early inflammatory marker indicates that YKL-40 could possibly correlate with other early markers of endothelial activation and/or dysfunction & inflammation as hsCRP [33].

Also, in the current study marked changes in the lipid profile was found in diabetic patients in the form of increased serum TG, total-C and LDL-C and decrease serum HDL-C in the three diabetic groups compared to the control group, with more dyslipidemic changes in patients with higher levels of albuminuria (macroalbuminuria).This is in accordance with previous studies which reported that diabetic patients with nephropathy have more marked

dyslipidemias (particularly low HDL-C and higher triglycerides) [49,50]. An established knowledge about impact role of lipid metabolism in early processing of atherosclerosis is well known. So, dyslipidemia is deleterious especially in diabetic patients [50].

Regarding retinopathy within diabetic patients, the study did not show any association between YKL-40 levels and the severity of retinopathy. This finding is in harmony with the finding of **Rathcke et al.**[33] who reached the same results. Diabetic patients especially those with micro and macro albuminuria frequently had higher prevalence of retinopathy as a part of low grade inflammation, endothelial dysfunction, and high evidence of retinal arteries atherosclerotic features. Also, this insignificant association between YKL-40 and the severity of retinopathy even in macroalbuminuria group is most likely to be explained by a systemically accentuated inflammatory state minimizing the individual impact of YKL-40 [33].

Finally, ROC curve analysis showed that, YKL-40 might be a good discriminator between patients with and without albuminuria. This is in accordance with previous studies recorded statistical significant association between YKL-40 and albuminuria in type II diabetic patients and demonstrated that serum YKL-40 level was a determinant of albuminuria independently of conventional risk factors [31, 51]. YKL-40 plays an important role in the process of diabetic nephropathy and atherogenesis via intermediating vascular endothelial dysfunction [51]. Albuminuria reflects vascular damage in the kidneys as part of systemic endothelial dysfunction [5]. Accordingly, serum YKL-40 level can be a good determinant of albuminuria in type II diabetic patients [31].

In **conclusion,** YKL-40 has emerged as a promising marker of inflammation and endothelial dysfunction that is involved in the pathogenesis of diabetic micro- and macroangiopathy. That finding suggests a role for YKL-40 in the gradually progressing vascular complications in patients with diabetes, with YKL-40 being a possible early and good marker of renal affection**.** It seems to be useful for screening because it is detectable in early stages and subclinical diseases.

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تقييم مستوي ال YKL-40 في مرضي البوال السكري من النوع الثاني مع ازدياد نسبه الزلال في البول

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الهدف من هذا البحث هو تقييم مستوي ال YKL-40 في مصل الدم لمرضي البوال السكري من النوع الثاني مع ازدياد نسبه الزلال في البول و كذلك اختبار علاقته مع البروتين سي المتفاعل عالي الحساسيه و مقاومه الانسولين لهؤلاء المرضي.

و قد اجريت هذه الدراسه علي ١٢٥ مريضا بالبوال السكري من النوع الثاني المترددين علي وحدة السكري و الغدد الصماء بمستشفي الباطنه التخصصي بالمنصوره. و قد تم تقسيم المرضي الي ثلاث مجموعات:

المجموعه الاولي:٣٩ مريضا معدل افراز الزلال في البول طبيعي (اقل من ٣٠ مليجرام/ ٢٤ساعه)

المجموعه الثانيه: ٤٦مريضا يعانون من زياده في معدل افراز الزلال في البول بنسبه ٣٠-٣٠٠مليجرام/ ٢٤ساعه

المجموعه الثالثه:٤٠مريضا يعانون من زياده في معدل افراز الزلال في البول بنسبه اكثر من ٣٠٠مليجرام/ ٢٤ساعه (اعتلال الكلي السكري).

المجموعه الضابطه شملت ٣٥من الاشخاص الاصحاء مع تجانس النوع و السن مع المرضي.

و قد اظهرت نتائج هذا البحث ان مستوي ال YKL-40 بمصل الدم قد ازداد في الثلاث مجموعات لمرضي البول السكري عن المجموعه الضابطه زياده ذات قيمه احصائيه عاليه. وقد اظهرت النتائج وجود ارتباط بينه و بين البروتين سي المتفاعل عالي الحساسيه و مقاومه الانسولين لهؤلاء المرضي. وايضا ثبت التحليل الاحصائى ال ROC curve ان ال YKL-40 يعد دلاله جيده للتفرقه بين وجود او عدم وجود الزلال في البول (درجه الحساسيه ٩٣% - درجه الخصوصيه ٨٨%)

و من نتائج هذا البحث نستنتج ان ال YKL-40 يعد دليل للالتهاب و الخلل في بطانه الاوعيه الدمويه. و ان مستواه قد ارتفع عند مرضي البول السكرى من النوع الثاني مع ملاحظه زياده كبيره في مجموعه مرضي البوال السكرى ذو الاعتلال بالكلي. وبالتالي فهذه النتائج تشير الي وجود دور لل YKL-40في الزياده التدريجيه لمضاعفات الاوعيه الدمويه عند مرضي السكرى، مع احتماليه كونه دليل جيد وجديد علي تاثر الكلي. و يبدو انه مفيد للكشف المبكر لانه يمكن قياسه في المراحل المبكره و المرحله قبل الاكلينيكيه للمرض.