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Assessment of Serum Interleukin-19 Level in Patients with Diabetic Nephropathy

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Interleukin-19 (IL-19) is a newly discovered cytokine belonging to the Interleukin-10 (IL-10) family. IL-19 has indispensable functions in many inflammatory processes and also can induce the angiogenic potential of endothelial cells. The purpose of present study was to assess the level of serum interleukin-19 (IL-19) in patients with diabetic nephropathy (DN).
Our Study Aimed to assess the level of serum IL-19 in patients with diabetic nephropathy.
Methods: In this cross-sectional study, we tested 90 subjects; 30 healthy control and 60 diabetic nephropathy patients recruited from outpatient clinics and wards of Internal Medicine department, Tanta university hospitals, Egypt. Patients were subdivided into 3subgroup according to the urinary albumin creatinine ratio (ACR).
Results: The serum IL-19 levels in DN patients were significantly higher than the control group. The mean serum IL-19 level was 15.45±4.34 Pg/ml, 32.66±8.05 Pg/ml, 56.03±7.89 Pg/ml and 71.41±12.37 Pg/ml dL for control, normoalbuminuria group, microalbuminuria group and macroalbuminuria group respectively.
Conclusions: Serum IL-19 level was significantly elevated in patients with diabetic nephropathy and was associated with the marker of inflammation CRP (C -reactive protein). So

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Keywords: Interleukin-19; diabetic nephropathy; urinary albumin creatinine ratio; C -reactive protein.

1. INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder with a lot of etiologies, characterized by hyperglycemia and disturbances of carbohydrate, fat and protein metabolism coming from defective insulin secretion, action of insulin or both. The long-term effects of diabetes are microvascular complications such as nephropathy, neuropathy and retinopathy [1].

Diabetic nephropathy (DN) represents a common, disabling, largely neglected problem affecting approximately 50% of patients with diabetes [2]. It is a major microvascular complication of diabetes mellitus; it is the leading cause of end-stage renal disease. Inflammation plays some important roles in the pathogenesis of DN. Leukocytes, macrophages and monocytes all are involved in the process of DN [3].

DN is a syndrome manifested by: persistent albuminuria, massive decrease in the glomerular filtration rate (GFR) and also rising arterial blood pressure (4). It is already the most common cause of DKD and ESRD, and is associated with cardiovascular morbidity and mortality. Oxidative stress, inflammation, and fibrosis appear to be the critical links in the pathogenesis of DN [5].

Albumin is measured as the earliest clinically detectable evidence of DN. According to urinary albumin creatinine ratio (ACR) which are listed [4]:

1) Normoalbuminuria: less than 30 mg/g.
2) Microalbuminuria: 30-300 mg/g.
3) Macroalbuminuria: >300 mg/g.

Proinflammatory cytokines are related to the pathogenesis of CKD, especially TNF-α, IL-1β, and IL19. IL-19, a member of IL-10 family, activates the signal transduction through receptor complex. It is indicated that IL-19 is involved in the pathogenesis of many processes like psoriasis, atherosclerosis, asthma and also in DN [6]. So in this study, we assessed the level of serum IL-19 in patients with diabetic nephropathy and its role in the development and progression of renal injury in those patients [7].

2. MATERIALS AND METHODS

2.1 Study Design

This is a cross sectional study conducted at outpatient clinics and wards of Internal Medicine department, Tanta university hospitals, Egypt.

The study was conducted in a period between June 2019 to June 2021.

2.2 Subjects

This study was carried out on 90 subjects, 60 type2 diabetic nephropathy patients and 30 healthy control. Patients were selected from outpatient clinics and wards of Internal Medicine department, Tanta university hospitals. The informed consent was taken from patients and control after study approval by the Local Ethical Committee, Tanta University hospitals, Egypt.

Subjects were divided into the following groups:

Group 1: 30 healthy subjects as a control group.
Group 2: 60 type2 diabetic patients which were divided into;
Subgroup A: 20 T2DM with normoalbuminuria [urinary albumin creatinine ratio (ACR) < 30 mg/g].
Subgroup B: 20 T2DM with microalbuminuria [urinary albumin creatinine ratio (ACR): 30-300 mg/g].
Subgroup C: 20 T2DM with macroalbuminuria [urinary albumin creatinine ratio (ACR) ≥300 mg/g].

2.3 Inclusion Criteria

4) Patients aged from 18 to 70 years.
5) Type2 diabetic patients.
6) Patients with diabetic nephropathy: -DN is characterized by a progressive increase of urinary albumin creatinine ratio (ACR) from normo- to micro- to macroalbuminuria with decline in the glomerular filtration rate (GFR).

2.4 Exclusion Criteria

1. Patients with T1DM.
2. Patients with history of diabetic ketoacidosis or hypoglycemic coma in the

past 3 months preceding the study.
3. Patients with urinary tract infection.
4. Patients with other causes of nephropathy like hypertensive nephropathy, analgesic nephropathy and contrast induced nephropathy.
5. Patients with decompensated liver disease.
6. Pregnant patients with gestational diabetes or pre-existing diabetes.

2.5 Methods

All patients in this study were subjected to:

Full history taking and thorough clinical examination, radiological investigations; pelvic abdominal ultrasound and laboratory investigations including: -

- Fasting ,2hpp blood glucose and HbA1c level.
- Renal function tests including S. Creatinine, B. Urea and estimated glomerular filtration rate [eGFR].
- Liver functions test including ALT, AST, S. Albumin and S. Bilirubin.
- Albumin / Creatinine ratio [ACR].
- Complete blood count [CBC].
- C-reactive protein.
- Serum interleukin 19 level.

2.6 Statistical Analysis of the Data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. We used Chi-square test for categorical variables, to compare between different groups, Monte Carlo correction test used for chi-square when more than 20% of the cells have expected count less than 5. We used Student t-test for normally distributed quantitative variables, to compare between two studied groups, ANOVA with repeated measures for normally distributed quantitative variables, to compare between more than two studied groups.

3. RESULTS

3.1 Base-Line Characteristics of Studied Main Groups & Subgroups

3.1.1 Demographic and clinical data

In the study, there was no significant difference between the studied groups as regard anthropometric parameter (age and sex) as shown in table (1,2).

Subgroup c had significantly higher BMI and duration of diabetes than other studied groups with P value (p=0.001) but that there was no significant difference between the studied groups as regard blood pressure as in Table 3.The result of our study illustrated a significant difference in the level of glycemic states (FBG,2hPP, HbA1C) in diabetic nephropathy patients in comparison with control group (p<0.001*) as there was a significant increase in blood glucose level in subgroup C compared to other groups as in Table 4.

The present study showed significant difference in serum creatinine, blood urea and estimated glomerular filtration rate [eGFR] in diabetic nephropathy groups in comparison with control group (p<0.001*) as the higher level of serum creatinine and blood urea were documented in the subgroup C compared to other groups. The lower level of estimated glomerular filtration rate [eGFR] in the subgroup C (mean =43.4±16.9) compared to subgroup B (mean =83.1±10.9) group, subgroup A (mean=96.6±7.8) and control group (mean =107±10.3) as in Table 5 and Fig. 1.

Table 1. Age distribution in studied groups

Age (years)	Group1	Group2		
	Control (n=30)	***Subgroup A* (n=20)**	***Subgroup B* (n=20)**	***Subgroup C* (n=20)**
Range	30-50	35-60	40-65	45-70
Mean ± SD	43.43±7.7	53.6± 8.19	54.2± 6.71	57.2±7.23
P value	0.44			

Non-significant p value > 0.05

Table 2. Sex distribution in the studied groups

Sex		Group1	Group2			Total (n=90)
		Control (n=30)	*Subgroup A* (n=20)	*Subgroup B* (n=20)	*Subgroup C* (n=20)	
Male	N	15	12	11	12	50
	%	50.0%	60.0%	55.0%	60.0%	55.5%
Female	N	15	8	9	8	40
	%	50.0%	40.0%	45.0%	40.0%	44.4%
Total	N	30	20	20	20	90
	%	100.0%	100.0%	100.0%	100.0%	100.0%
Chi-square	X^2	2.32				
	P	0.09				

** Significant p value < 0.05 non-significant p value > 0.05*

Table 3. The Clinical findings of the studied groups

Clinical findings		Group1	Group2			t. test	P Value
		Control (n=30)	*Subgroup A* (n=20)	*Subgroup B* (n=20)	*Subgroup C* (n=20)		
Duration of DM (years)	Range	-	5-12	7-13	9-25	13.6	<0.01*
	Mean ± SD	-	8.6±2.21	10.7±1.78	14.2±4.74		
BMI	Range	19.5-24.5	26-33	27-35	29-37	15.4	<0.01*
	Mean ± SD	21.9±1.8	27.4±2.6	28.3±2.3	30.9±1.8		
Systolic B/P (mm\hg)	Range	110-120	110-130	115-135	120-150	6.3	0.05
	Mean ± SD	115±4.9	117.2±7.8	122.1±6.7	126.5±7.9		
Diastolic B/P (mm\hg)	Range	80-85	75-85	70-85	75-95	2.61	0.05
	Mean ± SD	81.3±2.6	81.5±2.1	79.3±6	84.5±5.3		

** Significant p value < 0.05 non-significant p value > 0.05*

Table 4. Blood glucose level in studied groups

Blood glucose level		Group1	Group2			t. test
		Control (n=30)	*Subgroup A* (n=20)	*Subgroup B* (n=20)	*Subgroup C* (n=20)	
Fasting blood glucose (mg/dl)	Range	80-99	130-150	155-200	160-250	30.8
	Mean ± SD	86.36±13.1	136.7±8.53	177.15±20.1	186.7±28	
2hpp blood glucose (mg/dl)	Range	120-135	220-250	220-270	290-330	49.5
	Mean ± SD	128.6±5.5	234.5±34.4	250±17.7	316.2±10	
HbA1C (%)	Range	4.5-5	6.5-7	6.6-8	8.3-9	4.39
	Mean ± SD	4.6±0.32	6.67±0.75	7.5±0.75	8.69±0.23	
P value	<0.001*					

** Significant p value < 0.05 non-significant p value > 0.05*

Table 5. The kidney function tests in the studied groups

The kidney function tests		Group 1	Group 2			T. test
		Control (n=30)	*Subgroup A*(n=20)	*Subgroup B* (n=20)	*Subgroup C* (n=20)	
S.creatinine (mg/dl)	Range Mean ± SD	0.5-1.2 0.87±0.2	0.6-1.1 0.85±0.18	0.9-1.3 1.1±0.14	1.1-3.4 1.4±0.69	1.5
B.urea (mg/dl).	Range Mean ± SD	15-40 20.1±5.7	20-30 24.9±3.7	25-35 29.2±3.1	30-65 42.3±11.8	22.2
eGFR (ml/min/ 1.73m)	Range Mean ± SD	90-130 107±10.3	86-112 96.6±7.8	67-98 83.1±10.9	30-80 43.4±16.9	65.5
P value		<0.001*				

** Significant p value < 0.05*

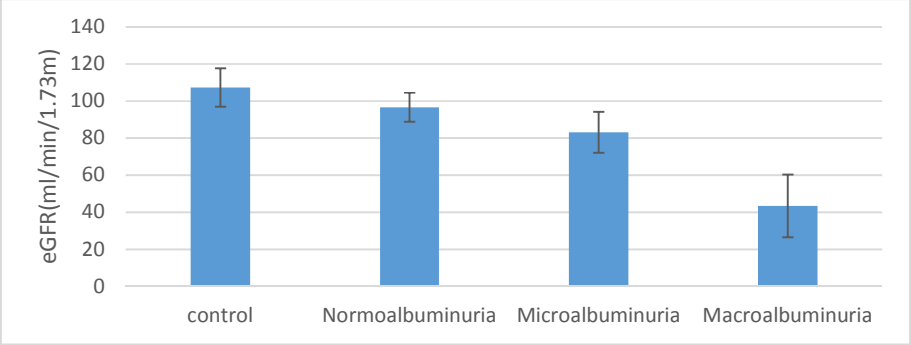

Fig. 1. eGFR level in the studied groups

3.2 Albumin to Creatinine Ratio (ACR) in the Studied Groups

The mean± SD of ACR level was 6.89 ±1.44 mg/g, 18.76±4.6 mg/g, 179.6±75.95 mg/g and 664.3±495 mg/g for group1, subgroup A, subgroup B and subgroup C respectively. Comparison between the studied groups showed that there was a significant increase in ACR ratio in the macroalbuminuria diabetic group compared to other groups as shown in Table 6 and Fig. 2.

3.3 C- Reactive Protein in the Studied Groups (CRP)

The mean ± SD of CRP level was 4.66 ± 0.83 mg/l, 7.75±1.16 mg/l ,12.7 ± 2.01 mg/l and 17.74 ±1.81 mg/l for group1, subgroup A, subgroup B and subgroup C respectively. Comparison between the studied groups showed that there was significant increase in CRP ratio in the subgroup C compared to other groups as shown in Table 7 and Fig. 3.

Table 6. Albumin to creatinine ratio (ACR) in the studied groups

ACR (mg/g)	Group 1	Group 2		
	Control (n=30)	*Subgroup A* (n=20)	*Subgroup B* (n=20)	*Subgroup C* (n=20)
Range Mean ± SD	5-9 6.89±1.44	11-29 18.76±4.6	50-290 179.6±75.95	320-2500 664.3±495
P value t. test	<0.001* 490.5			

TUKEY'S TEST	P1	P2	P3	P4	P5	P6
	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*

** Significant p value < 0.05; non-significant p value > 0.05; P_1: group I &subgroup A; P2: group I & subgroup B; P3: group1 & subgroup C; P4: subgroup A &; subgroup B; P5: subgroup A & subgroup C; P6: subgroup B & subgroup C*

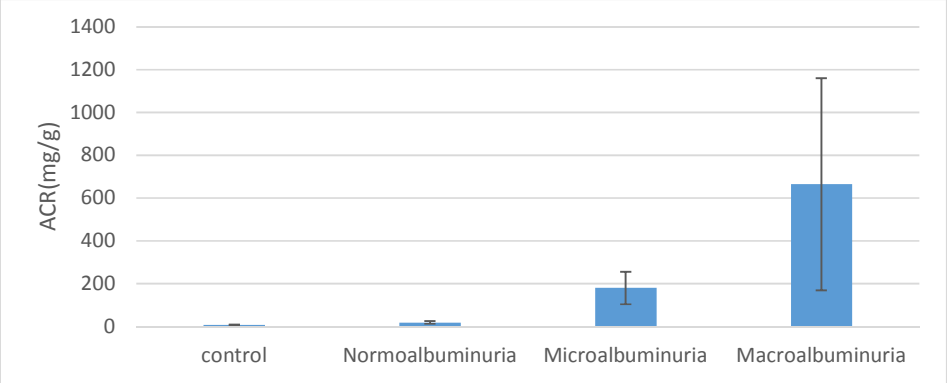

Fig. 2. Albumin to creatinine ratio in the studied groups

Table 7. C- reactive protein in the studied groups (CRP)

CRP (mg/l)	Group 1			Group 2		
	Control (n=30)		***Subgroup A* (n=20)**	***Subgroup B* (n=20)**		***Subgroup C* (n=20)**
Range	3-5		6-10	10-15		15-20
Mean ± SD	4.66±0.83		7.75±1.16	12.7±2.01		17.74±1.81
TUKEY'S TEST	P1	P2	P3	P4	P5	P6
	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
P value t. test	<0.001* 13.42					

** Significant p value < 0.05; non-significant p value > 0.05; P_1: group I &subgroup A; P2: group I & subgroup B; P3: group1 & subgroup C; P4: subgroup A &; subgroup B; P5: subgroup A & subgroup C; P6: subgroup B & subgroup C*

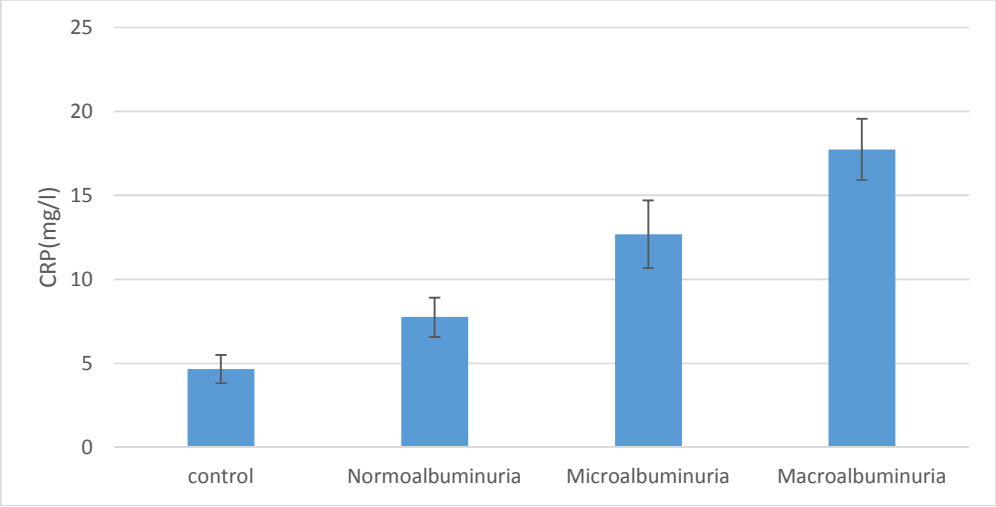

Fig. 3. CRP in the studied groups

3.4 Serum IL19 level

The mean serum IL-19 level was 15.45±4.34 Pg/ml, 32.66±8.05 Pg/ml, 56.03±7.89 Pg/ml and 71.41±12.37 Pg/ml dL for group1, subgroup A, subgroup B and subgroup C respectively. Comparison between the studied groups showed that there was a significant increase in serum IL-19 level in the subgroup C compared to other groups as shown in Table 8 and Fig. 4.

Table 8. IL19 level in the studied groups

IL19 (pg/ml)	Group 1	Group 2				
	Control (n=30)	*Subgroup A* (n=20)		*Subgroup B* (n=20)		*Subgroup C* (n=20)
Range	8.23-22.65	23.09-48.08		38.44-65.19		60.21-85.77
Mean ± SD	15.45±4.34	32.66±8.05		56.03±7.89		71.41±12.37
t. test	64.7					
P value	<0.0001*					
TUKEY'S TEST	P1	P2	P3	P4	P5	P6
	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*

** Significant p value < 0.05; non-significant p value > 0.05; P1: group I &subgroup A; P2: group I & subgroup B; P3: group1 & subgroup C; P4: subgroup A &; subgroup B; P5: subgroup A & subgroup C; P6: subgroup B & subgroup C*

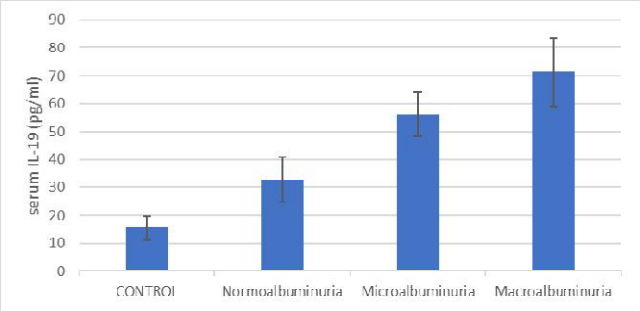

Fig. 4. Serum IL19 level in the studied groups

3.5 Correlations between Serum Il-19 Level and Other Parameters in the Diabetic Patients

There was significant positive correlation between serum IL-19 and fasting blood glucose, 2HPP blood glucose, HbA1C, S.creatinine, B.urea, ACR and CRP level between the diabetic patients.

There was negative correlation between serum IL-19 and eGFR level and also between serum IL-19 and serum albumin level between the diabetic patients.

Table 9. Correlations between serum Il-19 level and other parameters in the diabetic patients

Diabetic patients n (60)	Serum Il-19	
	R	P
Age (years)	0.12	0.34
BMI	0.71	<0.01*
Duration of DM (years)	0.51	<0.01*
Systolic blood pressure(mm\hg)	0.89	0.05
Diastolic blood pressure (mm\hg)	0.61	0.05
Fasting blood glucose (mg/dl)	0.25	<0.001*
2HPP blood glucose (mg/dl)	0.52	<0.001*
HbA1c (%)	0.41	<0.0001*
S.creatinine(mg/dl)	0.6	<0.001*
B.urea(mg/dl)	0.78	<0.001*
eGFR (ml/min/1.73m)	-0.79	<0.001*
ALT (U/L)	0.17	0.17
AST (U/L)	0.02	0.84
Total bilirubin (mg/dl)	0.22	0.07
Serum albumin (gm/dl)	-0.18	<0.01*
ACR (mg/g)	0.85	<0.001*
CRP (mg/l)	0.73	<0.001*

** Significant p value < 0.05; non-significant p value > 0.05*

Table 10. Univariate and multivariate logistic regression analysis in patients with diabetic nephropathy

	Univariate		Multivariate	
	OR (95% CI)	**P value**	**OR (95% CI)**	P value
BMI	0.325 (0.189 – 0.653)	0.001*	0.634 (0.298 – 0.982)	0.008*
Duration of DM (years)	0.489 (0.215 – 0.831)	0.005*	0.745 (0.364 – 0.831)	0.031*
Fasting blood glucose (mg/dL)	0.741 (0.621 – 0.931)	0.028*	0.631 (0.418 – 6.527)	0.138
2HPP blood glucose (mg/dL)	0.397 (0.215 – 0.745)	0.001*	0.581 (0.318 – 0.824)	0.006*
HbA1c (%)	0.564 (0.325 – 0.846)	0.019*	0.759 (0.527 – 4.329)	0.105
S. Creatinine (mg/dL)	0.458 (0.146 – 0.754)	0.001*	0.318 (0.068 – 0.627)	0.002*
B. urea (mg/dL).	0.648 (0.312 – 0.957)	0.001*	0.451 (0.268 – 0.751)	0.005*
eGFR (ml/min/1.73m)	2.635 (1.874 – 5.632)	0.001*	3.604(1.397 – 9.507)	0.001*
Serum albumin (gm/dL)	5.362 (3.159 – 11.685)	0.034*	2.604 (0.567 – 7.325)	0.249
ACR (mg/g)	0.749 (0.534 – 0.832)	0.001*	0.254 (0.103 – 0.537)	0.001*
CRP (mg/l)	0.594 (0.267 – 0.845)	0.001*	0.437 (0.134 – 0.659)	0.002*

Table 11. ROC curve of serum IL-19 between the diabetic groups

(ROC) curve	Cutoff	Area under curve	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Serum 1L-19 (pg/ml)	48	0.962	95	88	80	97	90

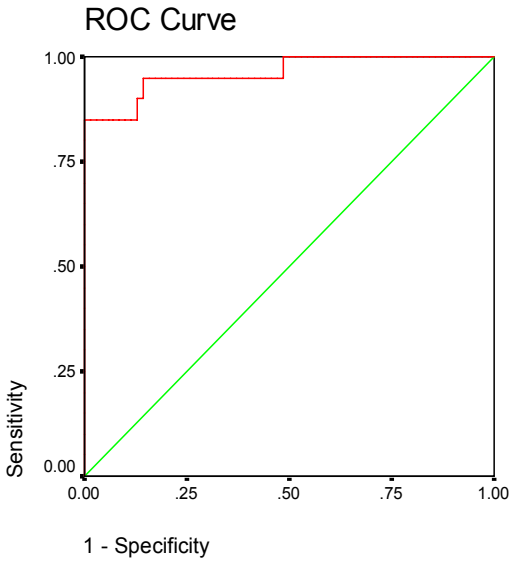

Fig. 5. ROC curve of serum IL-19 between diabetic patients

3.6 Univariate and Multivariate Analysis for the Prediction of Diabetic Nephropathy

In univariate analysis: BMI (p value 0.001*), duration of DM (p value0.005*), fasting blood glucose (p value0.028*), 2HPP blood glucose level (p value 0.001*), kidney function tests (p value 0.001*), ACR (p value 0.001*) and CRP was significant (p value 0.001*). They were all correlated with the prediction of diabetic nephropathy.

In multivariate analysis using model adjusted for previously mentioned level of serum IL-19 was significant and positive independent for prediction of diabetic nephropathy as in Table 10.

3.7 Receiver Operating Characteristic (ROC) Curve of Serum IL-19 between the Diabetic Patients

It was found that the best cut off value of serum IL-19 at 48pg/ml for prediction of diabetic nephropathy with area under curve (AUC) 0.962, sensitivity 95%, specificity 88% with positive predictive value 80% and negative predictive value 97% as shown in Table 11 and Fig. 5.

4. DISCUSSION AND CONCLUSION

Proinflammatory cytokines play an important role in the establishment of arteriolosclerosis and kidney injury especially DN. IL-19 which is a member of the IL-10 family and shares 20% amino acid identity with IL-10, but does not engage the IL-10 receptor [8].

Our results showed that there was a significant increase in duration of DM especially in the macroalbuminuria group (mean=14.2±4.74) than normoalbuminuria group (mean=8.6±2.21) and microalbuminuria group (mean=10.7±1.78) ($p < 0.01$*).

In agreement with our result Nishikawa et al., [9] who reported that a long duration of diabetes and poor glycemic control is associated with increased production of glycosylation end products, metabolic derangements, endothelial injury and oxidative products.

As regard BMI there was a significant increase in diabetic nephropathy patients than control group ($p < 0.01$*). There was a significant increase in BMI in the macroalbuminuria group (mean = 30.9±1.8) than the microalbuminuria group (mean = 28.3±2.3) and the normoalbuminuria group (mean =27.4±2.6) compared to control group (mean = 21.9±1.8).

Our study agrees with Klessens et al., [10] who found that obesity-associated glomerular hyperfiltration, renal vasodilation, increased glomerular filtration rate and intraglomerular capillary pressure and also high blood pressure are characteristics of DN.

The result of our study illustrated a significant difference in the level of glycemic states (FBG,2hPP, HbA1C) in diabetic nephropathy patients in comparison with control group ($p<0.001$*). Also, there was a significant increase in HbA1C in the macroalbuminuria group (mean = 8.69±0.23) compared to micro albuminuria (mean =7.5±0.75), normoalbuminuria group (mean = 6.67±0.75) and control group (mean = 4.6±0.32).

This is in agreement with I-Ching Kuo1 et al., [11] who found that hyperglycemia is the driving force for the development of DN.

The present study showed significant difference in serum creatinine, blood urea and estimated glomerular filtration rate [eGFR] in diabetic nephropathy groups in comparison with control group ($p<0.001$*) as the higher level of serum creatinine and blood urea were documented in the macroalbuminuric group compared to other groups. The lower level of estimated glomerular filtration rate [eGFR] in the macroalbuminuria group (mean =43.4±16.9) compared to microalbuminuria (mean =83.1±10.9) group, normoalbuminuria group (mean=96.6±7.8) and control group (mean =107±10.3).

In agreement with our result Frederik Persson et al., [12] reported that DN can lead to progressive proteinuria, focal glomerulosclerosis, severe mesangial matrix expansion, GBM thickening and later on nodular glomerulosclerosis and arteriolar hyalinosis.

The present study showed significant difference between diabetic nephropathy groups and control group as regard of albumin / creatinine ratio [ACR] ($p<0.01$*) as there was a significant increase in ACR ratio in the macroalbuminuria diabetic group (mean=664.3±495) compared to microalbuminuria group (mean=179.6±75.95), normoalbuminuria group (mean=18.76±4.6) and control group (mean =6.89 ±1.44).

In agreement with our result Yi-Chih Lin, et al., [13] reported that a significant increase in albumin / creatinine ratio [ACR] in diabetic nephropathy groups than control group especially in the microalbuminuria group. The explanation for elevation of ACR ratio that thickening of the glomerular basement membrane (GBM). After renal damage, the thickening of the basement membrane starts, which leads to pathologic modifications in mesangial and vascular cells. It leads to activation of the inflammatory pathway playing a significant role in the damage of GBM. This is complemented by the onset of microalbuminuria. Microalbuminuria is considered the first sign indicating the onset of DN.

As regard C-reactive protein (CRP) level, there was a significant difference between the diabetic nephropathy groups and control group

(p<0.001*) as there was a significant increase in the level of CRP macroalbuminuria group (mean=17.74±1.81) compared to microalbuminuria group (mean=12.7 ± 2.01), normoalbuminuria group (mean =7.75±1.16) and control group (mean 4.66 ±0.83).

Our findings agree with Gumuslu S, et al., [14] who documented that higher CRP levels in diabetic nephropathy groups especially in the macroalbuminuric group as inflammation plays a central role in the pathogenesis of DN and most recent studies have shown that C-reactive protein (CRP), the most extensively studied inflammatory marker, is associated with diabetic nephropathy patients. CRP which is a marker of inflammation, has been reported to be associated with the risk of DM complications and may deteriorate the inflammatory cascade in tissue injury in addition to initiating endothelial damage and atherosclerosis.

Our study showed a significant increase in serum interleukin (IL-19) level in diabetic nephropathy groups than control group (p <0.01*). There was a significant increase in the level of serum interleukin (IL-19) especially in the macroalbuminuria group (mean=71.41±12.37) than microalbuminuria group (mean=56.03±7.89) and normoalbuminuria group (mean= 32.66±8.05) compared to control group (mean =15.45 ±4.34).

In agreement with Li Li et al., [15] indicated that IL-19 plays an important role in the pathogenesis of DN. Elevated levels of IL-19 may be the result of pre-existing atherosclerosis in T2DM patients especially with macroalbuminuria and also elevations of CRP and serum IL-19 may directly alter glomerular function and thus be causally involved in the development of albuminuria. Multivariable logistic regression analysis showed that IL-19 levels were independently associated with DN. These results suggest that IL-19 is involved in the inflammatory reaction and can play a significant role in development and progression of DN.

Our result is also agreed with Li Li et al., [16] study who found that significant elevated in serum interleukin (IL-19) in patients with diabetic nephropathy who are at risk for microvascular and macrovascular lesions indicating that there is a potential link between IL-19 and glomerular function. IL-19 may influence the metabolism of the vascular endothelium and the glomerular basement membrane and is involved in the etiology of microalbuminuria. IL-19 could emerge with a direct role in the acceleration of vascular injury, in addition to the pro-inflammatory effect on this pathophysiology of DN.

Our data showed that there was a significant positive correlation between serum interleukin (IL-19) and (FBG,2hPP, HbA1C) and also between serum interleukin (IL-19) and albumin / creatinine ratio [ACR] which is a marker of renal injury but there was a negative correlation between serum interleukin (IL-19) and estimated glomerular filtration rate levels.

It agrees with Fujita T et al., [17] suggested that hyperglycemia is considered be the cause for the development of DN. Our explanation is that long term hyperglycemia may increase the level IL-19 via stimulating endothelial cells, which lead to local inflammation and endothelial damage of renal cell and atherosclerosis can also occurs.

Moreover, there was also a positive correlation between serum interleukin (IL-19) and CRP and it agreed with Liu Q et al., [18] found that CRP may deteriorate the inflammatory cascade in tissue injury in addition to initiating endothelial damage and atherosclerosis.

Our results showed that using univariate and multivariate logistic regression analysis in patients with diabetic nephropathy, serum IL-19 was significant and positive independent for prediction of diabetic nephropathy.

Our results were in accordance with El hefnawy KA et al., [19] who reported that IL-19 levels are independently associated with patients with DN.

CONSENT

It is not applicable.

COMPLIANCE WITH ETHICAL STANDARDS

Disclosures “Drs, Mariam Abd El wahed Attia, Yasser Mostafa Hafez, Maaly Mohamed Mabrouk, Medhat Abd El Megeid Ghazy have no conflicts of interest or financial ties to disclose. As per international standard or university standard written ethical approval has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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