Relation of C-Reactive Protein with Age and BMI in Diabetic Foot Patients

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Abstract

Diabetes mellitus (DM) is a chronic disease cannot be cured, and is a combined with serious complications especially after 10-20 years .Diabetic foot (DF) is one of severe diabetes mellitus complications and include ulcers and infection of feet. C-reactive protein(C-RP) is an acute-phase protein, rises in the blood as response to infection.The aim of this study is to assessment of C-reactive protein in diabetic foot patients and its relationship with Age and BMI in a sample of Iraqi patients with type2 diabetes mellitus.The study included twenty five (25) diabetic foot patients aged (36-77 years) with type 2 DM (duration ranged from 2-31 years) compared with twenty five patients aged (43-76 years) with type 2 DM without diabetic foot (duration ranged from 1-32 years) as patients control group and thirty (30) healthy subjects aged(42-80 years) as healthy normal control group.Fasting blood glucose and hs-CRP were determined in patients and control groups. C-RP concentrations were assessed by using the Enzyme linked Immunosorbent Assay (ELISA) method.

Results: The patients with diabetic foot lesions were found to be poorly controlled and had significantly higher levels of fasting blood glucose (FBG) ($p<0.001$) compared to patients without diabetic foot lesions and control groups. The patients with diabetic foot lesions were found to had significantly higher levels of C-RP ($p<0.001$) compared to patients without diabetic foot lesions and control groups. CRP levels were significantly increased in diabetic foot patients with increase of age and body mass index (BMI).

Conclusion: Increasing of infection ability according to increasing of age and BMI for diabetic foot patients.

Key words: C-reactive protein, Age and BMI, Diabetic foot.

علاقة البروتين الفعال –C (C-RP) مع العمر ودالة كتلة الجسم (BMI) في مرضى القدم السكري

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الخلاصة

مرض السكري هو مرض مزمن لا يمكن شفاءه وله مضاعفات خطيرة خصوصا بعد مرور 10- 20 سنة من ظهور المرض . ان مرض القدم السكري هو احد مضاعفات مرض السكري الخطيرة والذي يشمل قروح والتهاب الاقدام. ان CRP هو بروتين يزداد في الدم كاستجابة للالتهاب.

هدف الدراسة هو تقدير مستوى CRP في مرضى القدم السكري وعلاقتها بالعمر ودالة كتلة الجسم عند المرضى العراقيين المصابين بداء السكري .تشمل الدراسة 25 من مرضى القدم السكري اعمارهم 36-77 سنة ذوي مدة اصابة بالسكري 2-31 سنة تمت مقارنتهم مع 25 من مرضى السكري بدون قدم سكري اعمارهم 43-76 سنة ذوي مدة اصابة بالسكري 1-32 سنة كمجموعة مرضى ضابطة للمقارنة و 30 شخص كمجموعة اصحاء ضابطة للمقارنة.

تم تقدير مستوى السكر الصيامي و CRP في دم المرضى والاصحاء، وتم تقدير مستوى CRP باستخدام تقنية الاليزا.

اظهرت النتائج وجود ارتفاع معنوي في مستوى سكر الدم وال CRP لمرضى القدم السكري مقارنة مع مرضى السكري بدون قدم سكري والاصحاء . وان CRP يزداد بزيادة العمر ودالة كتلة الجسم لمرضى القدم السكري.

الاستنتاج: زيادة قابلية الالتهاب(CRP يزداد) بزيادة العمر ودالة كتلة الجسم لمرضى القدم السكري.

الكلمات المفتاحية: البروتين الفعال-C ، العمر ودالة كتلة الجسم، القدم السكري.

Introduction

The diabetes mellitus (DM) is a chronic metabolic disorder characterized by increase concentrations of glucose in the blood above normal levels "hyperglycemia" with disturbances of metabolism for carbohydrates, lipids and proteins resulting from defects in secretion of insulin, action of insulin or both[1]. The high levels of blood glucose lead to macro and micro vascular diseases. Macrovascular diseases cause cardiovascular disease such as atherosclerosis and heart ischemic[2].

The microvascular diseases is damage the small blood vessels when coated with sugar which lead to retinopathy with affects blood vessels of retina of eyes and also can lead to nephropathy (damage of kidney), while the impact of diabetes on the nervous system causing

diabetic neuropathy which accompanied with numbness, tingling, and pain in the feet. Also diabetes increasing the risk of skin damage due to altered sensation. Neuropathy and vascular diseases in the legs are the risk factors of the problems related to diabetic foot, such as diabetic foot infections and ulcerations that difficult to treated and occasionally lead to amputation[3,4].

C-RP has a role as part of systemic immune response to inflammation by infectious, acute injury or other stimuli. C-RP binds to molecules have specific structures typically found in the case of cell death and also present on the surface of pathogens, therefore C-RP concentrations rapidly increased after injury of tissue or infections and its level reflects the intensity of the inflammation[5,6].

Materials and Methods

1- Subjects

Eighty (80) subjects were included in this study, and they were divided into 3 groups:

· Group I; Diabetic foot group: including 25 type 2 diabetic patients with diabetic foot lesions . Diabetes duration ranged from 2 to 31 years. The age ranged from 36 to 77 years, and they were compared with:

· Group II; Diabetic group: including 25 patients with type 2 diabetes. Diabetes duration ranged from 1 to 32 years. The age ranged from 46 to 68 years.

· Group III; Control group: comprising 30 apparently healthy persons which matched with age and sex as the diabetic patients. They were with no characterized diseases or endocrine disturbances. Clinically they were free from any abnormality.

The patients and healthy subjects gave information for the study, which was approved by National center of diabetes, Al-Mustansiryah university, Baghdad, Iraq. The parameters were recorded in the study are age, BMI, Waist Circumference (WC), and gender. The calculation of BMI was by dividing weight to height squared (kg\ m^2). The abnormal cutoff point of BMI was 25 kg\ m^2 [7]. Measurement of waist circumference (WC) was at the level midway between the lower rib margin and the iliac crest with the subject standing [8].

Blood specimens were collected for all cases after 8-12 h overnight fasting. The collection venous blood was in plastic tubes without additive, and the collected blood was allowed to clot for 30 min at room temperature then centrifuged at 3000 rpm for 10 min to get serum for immediate measurement of glucose. The remaining serum of the diabetic patients and healthy

Fasting plasma glucose was determined by using the method of Barham and Trinder (1972)[9] . C-RP concentrations were assessed by using the C-RP Enzyme linked Immunosorbent Assay (ELISA) kit (Demeditec diagnostics Gmbh.Lise-Meitner-StraBe2, Germany). Procedure was done according to the instructions of kits manufacturers.

The statistical analysis was done with Statistical Package for the Social Science for Windows (SPSS) and the results were expressed as the mean ± SD. To compare the difference among the groups, post hoc testing was performed by the Bonferroni test. The p value less than 0.05 were considered statistically significant [10].

Results

The values of parameters that characterized of the studied groups were summarized in Table 1,2,3,4. The diabetic studied groups were compared to control group. The patients and controls were age matched ($p>0.05$). No significant difference was detected between diabetic group and control group in WC ($p>0.05$). Also it was no significant difference detected between diabetic groups and control group in BMI ($p>0.05$) as shown in table 1.

Table 1: Values of some parameters for the studied subjects

Parameter		Diabetic foot		Diabetic		Control		P value
		No	%	No	%	No	%	
Age (years)	<50	5	20.0	4	16.0	11	36.7	0.072
	50—59	8	32.0	9	36.0	14	46.7	
	=>60	12	48.0	12	48.0	5	16.7	
	Mean± SD (Range)	58.12±9.29 (36-77)		59.60±9.27 (43-76)		53.13±8.61 (42-85)		
BMI (Kg/m2)	Normal (18.5-24.9)	5	20.0	4	16.0	7	23.3	0.563
	Overweight (25-29.9)	11	44.0	7	28.0	8	26.7	
	Obese (=>30)	9	36.0	14	56.0	15	50.0	
	Mean± SD (Range)	28.84±3.88 (22.6-36.3)		31.79±5.84 (23.6-45.1)		29.44±5.11 (20.2-40.4)		
Weight	Mean± SD (Range)	80.44±11.68 (60-105)		83.28±15.58 (60-114)		78.67±15.09 (55-120)		
Height	Mean± SD (Range)	1.65±0.07 (1.47-1.75)		1.62±0.08 (1.50-1.77)		1.66±0.08 (1.50-1.77)		
Waist (cm)	<100	6	24.0	5	20.0	12	40.0	0.09
	100—109	13	52.0	10	40.0	5	16.7	
	110-119	3	12.0	3	12.0	11	36.7	
	=>120	3	12.0	7	28.0	2	6.7	
	Mean± SD (Range)	106.1±11.56 (90.0-143.0)		107.0±12.10 (89.0-137.0)		104.9±12.07 (79.0-127.0)		
-Data were presented as Mean± SD (Range)								

FPG was significantly higher in the studied diabetic foot patients group compared to control groups as represented by $p<0.05$.It was also seen significant difference between diabetic foot patients and without diabetic foot patients($p<0.05$) as shown in table 2.

CRP was measured in three groups and showed significantly higher levels in diabetic foot patients than diabetic patients and control. C-RP was significantly higher in the studied diabetic foot patients group compared to control groups as represented by $p<0.05$, but it was no significant difference seen between diabetic patients without diabetic foot and healthy group ($p<0.05$) as shown in table 2,3.

Table 2: Mean± SD (Range) 0f FPG and C-RP for patients and control groups.

Parameter	Diabetic foot	Diabetic	Control	P value
FPG (mg/100 ml)	229.84±92.38* (95.0-443.0)	193.68±62.53* (114.0-386.0)	96.23±9.03 (80.0-120.0)	0.0001*
hs-CRP	14.00±12.61* (3.87-35.37)	4.83±4.02 (2.54-5.34)	3.89±4.21 (0.27-5.03)	0.0001*
-Data were presented as Mean±SD (Range) *Significant using ANOVA test at 0.05 level				

Table 3: Statistical of C-RP for patients and control groups.

Parameter		Diabetic foot	Diabetic	Control
hs-CRP	Number	25	25	30
	Mean	14.00	4.83	3.89
	Standard Deviation	7.61	2.02	1.21
	Standard Error of Mean	2.52	0.804	0.769
	P value compared to control	0.001*	0.405	-
	P value compared to diabetic	0.001*	-	-
*Significance at 0.05 level of significance				

Table 4 showed significant increase of C-RP in diabetic foot patients with increase of age, BMI and Waist Circumference (WC).

Table 4: CRP (Mean± SD) distributed according to age group and BMI for patients and control groups.

Parameter		hs-CRP (Mean± SD)					
		Diabetic foot		Diabetic		Control	
Age (years)	<50	5	7.0±7.2*	4	4.4±3.8	11	1.2±1.3
	50—59	8	15.0±14.2*	9	4.7±3.8	14	2.13±2.5
	=>60	12	16.6±13.1*	12	4.9±4.5	5	4.2±3.2
BMI (Kg/m2)	Normal	5	10.0±8.4*	4	2.3±2.7	7	1.8±0.4
	Overweight	11	14.2±10.0*	7	4.1±4.4	8	2.2±1.0
	Obese	9	21.1±13.1*	14	5.9±4.0	15	4.2±4.9
Waist (cm)	<100	6	7.6±6.0*	5	1.1±0.6	12	1.3±1.0
	100—109	13	13.2±10.2*	10	5.0±3.9	5	3.3±1.9
	110-119	3	19.3±9.8*	3	6.3±3.6	11	3.9±2.5
	=>120	3	24.9±14.9*	7	5.8±4.3	2	4.3±2.6

Discussion

Type 2 diabetes is characterized by hyperglycemia and dyslipidemia which associated with a cluster of risk factors forming the metabolic syndrome and leads to serious complications[11]. High levels of glucose leads to macro and micro vascular diseases. Cardiovascular diseases are the cause of death up to 80% of patients with type2 diabetes [12]. In this study, the levels of blood glucose was significantly higher in the diabetic patients than blood glucose of control (table 2), and that showed that the diabetic patients often with poor (bad) glycemic control. Statistical significant elevated of CRP levels were detected in patients with diabetic foot ulcer compared with those in patients without foot ulcers and healthy control groups ($P < 0.05$). High levels of CRP in diabetic foot patients agreed with fact that most of lesions are infected because wounds are an ideal place for bacteria to colonize and proliferative since raw tissue and serous exudate provide an excellent medium for bacterial growth[13]. This result agreed with many of previous studies[6]. CRP is a member of the oligomeric proteins involved with recognition in innate immunity and it is a principal

downstream mediator of the acute phase response. Immunoregulatory roles of CRP include enhanced of leucocytes reactivity, complement fixation, modulation of platelet activation, and clearance of cellular debris from sites of active inflammation[14]. CRP can mediate activation of monocytes and macrophages and other cytokines, and assist in the complement pathway[15]. Previous studies have been postulated that Type II diabetes may represent a disease of the innate immune system[14].In this study CRP was increased in diabetic foot patients with increase of age and BMI and this refers to that the ageing and increase body weight in diabetic foot patients make them more prone to infection. As response to acute and chronic inflammatory conditions C-RP levels are increase in the plasma of blood, making it a useful measure of inflammation. The C-RP levels increases rapidly after infections or tissue injury and its levels reflects the intensity of the inflammation [5,6] .

Conclusion

Increasing of infection ability in diabetic foot patients according to increasing of age and BMI

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