Association of C reactive Protein with Type-2 Diabetes Mellitus (T2DM) and Obesity: A Case- Control Study

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Abstract

This study assesses the association of C-reactive protein (CRP) with type-2 diabetes mellitus (T2DM) and to determine the effect of obesity on them in the population of Amin-Hayat diabetic center in Lahore. We included 130 women and 120 women at baseline (2020–2021). Blood samples and epidemiological data were collected. Physician-diagnosed T2DM subjects (60women and 50 men) were self-reported or based on fasting glucose ≥125mg/dL during follow-up of 2 years between 2020 and 2021. After multivariate adjustment for T2DM risk factors, we observed that CRP and glucose level was significantly higher in obese subjects when compared with overweight, normal weight and underweight subjects (p <0.05).

Keywords: C-reactive protein; Type-2 diabetes mellitus; Body mass Index

Background

Type 2 Diabetes Mellitus is a global health problem. Many inflammatory proteins are produced during the development of T2DM [1]. But C reactive protein is a major inflammatory marker of the T2DM, which is produced by liver cells [2]. High level of this marker has been associated with hypertension, obesity, smoking and drinking [3-7]. This sensitive inflammatory marker may be a predictor of cardiovascular disease [8-10]. Therefore, for preventive measures early detection of elevated CRP and identification of factors associated with this are important [11]. Mostly, studies have been conducted on the Western populations, very small number of studies have been done on the Asians. The aim of our study is to assess the relationship of CRP with T2DM and examine the factors associated with elevated CRP among newly diagnosed T2DM patients.

Methodology

- **Study Population:** We conducted this cross-sectional study on 250 newly diagnosed diabetic patients who attended the Amin-Hayat diabetic center in Lahore from Jan 2020 to June 2021. Among 250 subjects 120 were males and 130 were females with age range 40-65 years. The subjects included in the study were belonging to low socioeconomic status.
- **Data Collection:** All participants underwent a physical examination and detailed interview. They were questioned by attendants regarding their life style and socio demographic status (i.e. age, gender, height, weight, waist circumference, dietry pattern, smoking or nonsmoking, blood pressure and family history of diabetes) and information relevant to study was achieved.
- **Body Mass Index (BMI):** The diabetic patients were categorized on the basis of BMI. BMI is defined as individual body weight is divided by the square of his or her height. The formula of body mass index produced a unit of measurement of Kg/ (m) ^{2}

SI BMI = Body Mass (Kg)/ (Height m) ^{2}

A BMI of <18.5 is considered as underweight while a number 18.5 to 24.9 is considered normal weight. BMI of 25to 29.9 is considered overweight. If individual is >30 then it suggests that the individual is obese [12].

- **Sample Collection:** From all participants, blood samples were collected after 8 hours of fasting. Both plasma and serum were separated and stored in 3 vials (300 ul/vial) in -80 ° C freezer.
- **Biochemical analysis:** Biochemical analysis was performed by the internist as a consultant diabetologist in the Amin Hayat diabetic center (Hitachi 902 biochemical analyzer). These biochemical tests included both fasting and random blood glucose levels, lipid profile test (triglyceride, cholesterol, and HDL and LDL tests).
- **CRP Measurement:** ELISA was used for the measurement of CRP levels. CRP levels were classified according to the guidelines of the Centers for Disease Control [13, 14].

Level of CRP less than 1 mg/l predicts low risk.

CRP level between 1 and 3mg/l predicts moderate risk.

Greater than 3 mg/l predicts high risk.

Greater than 100mg/l CRP level predicts acute phase of diabetes and heart disease.

Reference range for CRP in normal adults is 0.05-0.20 mg/l [15]. Patients with CRP level below this range were considered to be normal and patients above this range were considered diabetics.

Results

A total of 250 newly diagnosed type-2 diabetic participants (Males n= 120, Females n= 130) were analyzed in the present study. The baseline demographic and biochemical characteristics of participants were compared in males and females as shown in Table 1. No gender difference was observed in both demographic and biochemical characteristics. Subjects were stratified into four groups on the basis of BMI (kg/m^2) according to Asian standards. 9% subjects were included in the BMI group1 (underweight), 39% subjects were included in the BMI group2 (normal weight), 30% subjects were included in the BMI group3 (overweight) and 22% subjects were obese and included in the BMI group 4 (Figure 1). Demographic and biochemical characteristics of each BMI group were described in Table 2. We observed that random glucose level value was significantly higher in obese subjects when compared with overweight, normal weight and underweight subjects (p <0.05). (Tables 1, 2) (Figure 1)

Additionally, we analyzed the relationship between CRP and BMI groups. As shown in Table 2, there was significant association between CRP and BMI groups. CRP level was significantly higher in obese subjects (4.33±0.59 mg/l) compared to overweight (4±0.44 mg/l), normal (3.82±0.39 mg/l) and underweight (2.34±0.80 mg/l) subjects (p <0.05). Higher risk of elevated CRP was observed in participants of BMI 4 (obese) and BMI 3 (overweight) groups

Table 1: Demographic and Biochemical Characteristics of Study.

	Subjects		
Parameters	**All**	**Male**	**Female**
n	150	90	60
	mean ± SEM	mean ± SEM	mean ± SEM
Age (Years)	51.52±0.787	53.63±0.924	48.4±1.3
Height (cm)	166.8±1.21	170.2±1.67	161.4±1.47
Weight (kg)	69.08±1.14	73.42±1.36	62.58±1.69
BMI (Kg/m²)	25±0.458	25.7±0.54	25±0.811
Waist (cm)	97.69±0.962	96.83±1.35	98.98±1.29
Hip (cm)	97.28±0.738	96.51±0.99	98.43±1.07
WHR	1.002±0.008	1±0.01	1.003±0.008
Fasting Glucose(mg/dl)	195.93±4.58	196.7±5.6	194.87±7.82
Random Glucose(mg/dl)	286.83±4.34	283.62±5.49	295±7.08
Cholesterol (mg/dl)	189±3.74	186±4.96	192±5.7
Triglycerides (mg/dl)	223±112.65	225±10.6	204±16.8
HDL (mg/dl)	39.1±0.702	38.4±0.577	40±1.53
LDL (mg/dl)	121±2.84	118±3.62	125±4.55
CRP (mg/l)	3.86±0.26	3.90±0.34	3.8±0.43
*t´*test: p > 0.05, no gender differences were observed in the mean value of demographic and biochemical data.			

Table 2: Demographic and Biochemical Characteristics of Study subjects.

Parameters	**Underweight**	**Normal weight**	**Overweight**	**Obese**	**ANOVA**
	(n)	(n)	(n)	(n)	
	8	35	27	20	p-value
	mean ± SEM	mean ± SEM	mean± SEM	mean± SEM	
Age (years)	52.6± 1.84	50.3± 1.47	51.9± 1.25	52.7±1.38	
WHR (cm)	0.974± 0.016	1.02± 0.01	0.99± 0.009	2.96± 1.97	
Fasting glucose(mg/dl)	212.3± 14.5	192.8± 7.90	194.4± 7.41	198± 9.68	>0.05$^{N\text{-}S}$
Random glucose(mg/dl)	276.2± 16.8	278± 8.44	290.1±6.94	294.1±8.87	<0.05*
Cholesterol (mg/dl)	194.7±11.7	192± 5.74	189± 7.22	190± 8.64	>0.05$^{N\text{-}S}$
Triglyceride (mg/dl)	198± 20.5	216± 13.5	232±21.6	233± 15.8	<0.05*
HDL (mg/dl)	38.4± 1.91	39.4±0.8	39.57± 1.93	38.69±0.97	>0.05$^{N\text{-}S}$
LDL (mg/dl)	134.3±10.6	124±4.44	117.4± 5.61	114±5.17	>0.05$^{N\text{-}S}$
CRP (mg/l)	2.34±0.80	3.82± 0.39	4±0.54	4.33±0.59	<0.05*
* Significant		$^{N\text{-}S}$ Non-significant			

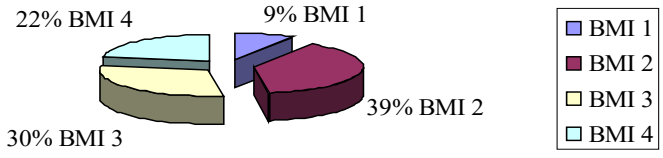

Figure 1: Percentage distributions of different BMI groups in study population.

BMI 1: Underweight subjects; **BMI 2:** Normal weight subjects; **BMI 3:** Overweight subjects; **BMI 4:** Underweight subjects

with no physical activity compared to BMI 2 (normal) and BMI 1 (underweight) groups with regular exercise and physical activities. Comparison of serum CRP concentration among different BMI groups has been shown in Fig 2. To assess the relationship of CRP with glucose level, we did correlation analysis of CRP and glucose level and we observed strong and significant correlation between CRP and glucose level (r = 0.98, p <0.01) (Fig 3). (Figure 2, 3)

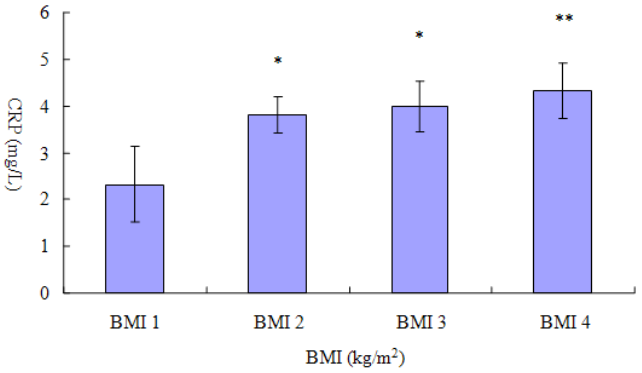

Figure 2: mean±SEM of the C - reactive protein among BMI groups.

BMI 1: Underweight subjects; BMI 2: Normal weight subjects; BMI 3: Overweight subject; BMI 4: Underweight subjects.

* Difference between the groups is significant (p < 0.05)

** Difference between the groups is highly significant (p < 0.01)

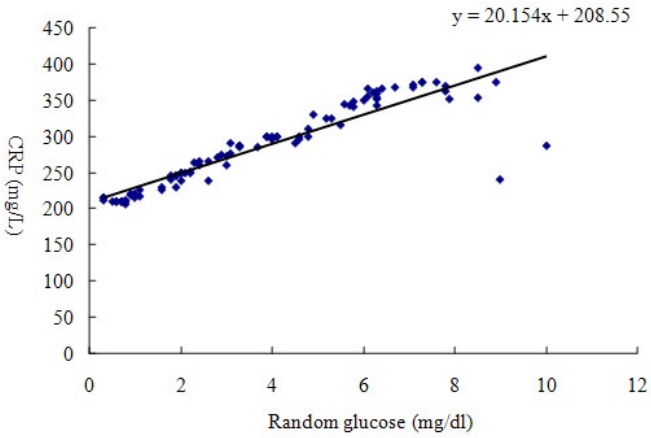

Figure 3: Correlation between serum CRP (mg/l) and Random glucose level (mg/dl).

Discussion

In this study, concentration of CRP was associated with developing T2DM and its risk factors. CRP and its relationship with obesity were associated with increased risk of developing T2DM.

CRP is an inflammatory marker which level is increased in the patients with severe inflammation and diseases including CVD and T2DM. Wen et al. studied a Chinese population and report that the CRP level was higher in patients of T2DM than normal subjects, and suggested that C reactive protein is an independent predictor of type 2 diabetes mellitus [16]. Many studies reported that elevated CRP is positively associated with increased risk of T2DM [4, 17, 18]. However, Pan et al. studied a Singapore population (571 T2DM subjects) and they reported that CRP was negatively associated with increased risk of T2DM [19].

CRP is a reliable and utilizable marker than other markers i.e. cytokines, because of its higher stability in plasma or serum and its ease of measurement [5]. Mechanism of the relationship between T2DM and CRP is not known in detail. However, some factors such as oxidative stress and genetic factors related to T2DM are explained in detail. In present study, we included a population of Amin Hayat Diabetic Hospital, and our results showed that CRP concentration varied by gender and metabolic parameters. Our analysis showed that elevated CRP concentration was associated with increased risk of T2DM. Moreover, CRP level was high in women than men. These results are consistent with many studies showing that elevated CRP concentration is strongly associated with T2DM [6, 17].

Most T2DM subjects are obese with higher insulin resistance and BMI [20]. It is thought that elevated CRP concentration induces insulin resistance through different mechanisms i.e. production of thrombogenic agent, complement cascade activation and enhancement of adhesion molecules [21, 22]. In this reference, we studied the association between CRP and T2DM in relation to obesity (BMI). Our analyses showed that obesity interact with the association between CRP and T2DM.

In the present study BMI was positively associated with the CRP and a strong risk factor for the occurrence of diabetes. We found that concentration of CRP increases with increasing BMI. CRP value is significantly higher in obese subjects and CRP value is significantly lower in underweight subjects. Similar results were also observed by many authors [20, 23]. They reported elevated CRP concentration among individuals who are obese or have diabetes and lower CRP level among individuals whose BMI is <18.5 kg/m2.

In conclusion, we found a strong positive association between CRP and T2DM in a population based study. These relationships were more prominent in obese and overweight patients. However, further studies on various populations are warranted for corroboration of our findings.

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