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TYPE 2 DIABETES MELLITUS; C-REACTIVE PROTEIN IN PATIENTS

Dr. Mukhtiar Hussain Jaffery[1], Dr. Nisar Ahmed Shah[2], Dr. Muhammad Sajid Abbas Jaffri[3], Dr. Athar Hussain Memon[4], Dr. Syed Zulfiqar Ali Shah[5]

1. FCPS
   Assistant Professor
   Department of Medicine
   Liaquat University of Medical and Health Sciences
   (LUMHS) Jamshoro
2. MD, Dip. Card
   Consultant Physician
   Department of Medicine
   Liaquat University Hospital
   Hyderabad
3. FCPS
   Associate Professor
   Department of Medicine
   Bahria University Medical & Dental College Karachi
4. 4th Year MBBS
   Chandka Medical College Larkana
5. Postgraduate
   Department of Medicine
   Liaquat University of Medical and Health Sciences
   (LUMHS) Jamshoro

Correspondence Address:
Dr. Syed Zulfiqar Ali Shah
House No: 279, Doctor's Colony
Hirabad, Hyderabad, Sindh, Pakistan
zulfikar229@hotmail.com

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ABSTRACT…Objective: To determine the frequency of raised C-reactive protein (CRP) in patients with type 2 diabetes mellitus. **Patients and methods:** This cross sectional descriptive study of six months study was conducted at Liaquat University Hospital Hyderabad from March 2013 to August 2013. All diabetic patients of ≥35 years age of either gender for >01 year duration visited at OPD were evaluated for C-reactive protein and their glycemic status by hemoglobin A1c. The data was analyzed in SPSS and the frequency and percentage was calculated. **Results:** During six month study period, total 100 diabetic patients were evaluated for C-reactive protein. Majority of patients were from urban areas 75/100 (75%). The mean ±SD for age of patients with diabetes mellitus was 51.63±7.82. The mean age ±SD of patient with raised CRP was 53±7.21. The mean ±SD for HbA1c in patients with raised CRP is 9.55±1.73. The mean random blood sugar level in patients with raised CRP was 247.42 ± 6.62. The majority of subjects from 50-69 years of age group with female predominance (p = 0.01) while the CRP was raised in 70(70%) patients in relation to age (p=0.02) and gender (p=0.01) respectively. Both HbA1c and CRP was raised in 64.9% (p = 0.04) in patients with type 2 diabetes mellitus. The mean ±SD of CRP was 5.8±1.21 while for male and female individuals with raised CRP was 3.52±1.22 and 5.7±1.63 respectively. **Conclusions:** The raised CRP was observed in patients with type 2 diabetes mellitus

Key words: Diabetes mellitus, C reactive protein, Hemoglobin A1c

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INTRODUCTION

Diabetes mellitus (DM) is metabolic disease and associated with long-term complications of various systems / organs of the body[1-7]. The study conducted on 5433 individuals in Pakistan shown 19% prevalence of diabetes mellitus[2].

C-reactive protein (CRP) is an acute phase protein synthesized by liver. The cytokines i.e. IL1, IL6 and TNF stimulate the CRP production in response to infection and inflammation[8,9]. It is the inflammatory marker associated with insulin resistance, cardiovascular diseases and type 2 diabetes mellitus[11]. It also plays a role in endothelial dysfunction and in metabolic syndrome[12]. The exact mechanism of insulin resistance is still unclear[10]. However, its close association with atherogenesis suggests that the effective and specific therapy may help to reduce the diabetes related macrovascular complications[13]. The high glucose, lipoproteins, FFA and adipokines released by endothelial and smooth muscle cells and macrophages are responsible for the production of CRP[14]. This study was conducted to evaluate the frequency of raised CRP among the patients of type 2 diabetes mellitus who presented at Liaquat University Hospital, Hyderabad.

PATIENTS AND METHODS

The study was carried out in the department of medicine at Liaquat University Hospital. All the patients of ≥35 year age, of either gender were known diabetes for ≥ 01 years duration visited at OPD for glycemic control and monitoring were entered in the study. The referral diabetic patients from different wards of hospital as well as inpatients were also taken and evaluated for C-reactive protein. The blood sugar and haemoglobin A1C (HbA1C) was also advised to evaluate the status of their diabetes i.e. control or poorly control. For the evaluation of CRP, 2cc venous blood was taken in a disposable syringe and sent to laboratory

for analysis. The normal reference range for C-reactive protein is 0-1.0 mg/dL while the level >1.0 mg/dL was considered as raised. The patients with rheumatic fever, different infectious diseases (meningitis, poliomyelitis, infectious mononucleosis, and syphilis), malignancy, rheumatoid & septic arthritis were excluded from the study. The informed consent was taken from patients and the data was recorded on proforma. The SPSS was used to analyze the data and the frequency, percentage and gender distribution was calculated as far as CRP was concerned. The mean ± SD was calculated for numerical variables. The chi square test was applied and the statistical significance was considered when the p-value ≤0.05.

RESULTS

During six month study period, total 100 diabetic patients were evaluated for C-reactive protein. Majority of patients were from urban areas 75/100 (75%). The mean ±SD for age of patients with diabetes mellitus was 51.63±7.82. The mean age ±SD of patient with raised CRP was 53±7.21. The mean ± SD for HbA1c in patients with raised CRP is 9.55±1.73. The mean ±SD of CRP was 5.8±1.21 while for male and female individuals having elevated CRP has 3.52±1.22 and 5.7±1.63 respectively. The mean random blood sugar level in patients with raised CRP was 247.42 ± 6.62. The age distribution in relation to gender & CRP is shown in Table-I and II while the gender in relation to CRP is shown in Table III. The HbA1c in relation to gender and CRP is shown in Table IV and V.

		GENDER		Total	P-value
		Male	Female		
AGE	35-39	4	5	9	
		11.4%	7.7%	9.0%	
	40-49	10	13	23	
		28.6%	20.0%	23.0%	
	50-59	12	17	29	
		34.3%	26.2%	29.0%	
	60-69	3	26	29	
		8.6%	40.0%	29.0%	
	70 +	6	4	10	0.01*
		17.1%	6.2%	10.0%	
Total		35	65	100	
		100.0%	100.0%	100.0%	

Table-I. The age distribution in relation to gender in patients with diabetes mellitus
**P-value is statistically significant*
Pearson Chi-square value = 12.09; df = 4

		CRP		Total	P-value
		Raised	Normal		
AGE	35-39	6	3	9	
		8.6%	10.0%	9.0%	
	40-49	12	11	23	
		17.1%	36.7%	23.0%	
	50-59	24	5	29	
		34.3%	16.7%	29.0%	
	60-69	18	11	29	
		25.7%	36.7%	29.0%	
	70 +	10	00	10	0.01*
		14.3%	00	10.0%	
Total		70	30	100	
		100.0%	100.0%	100.0%	

Table-II. The age distribution in relation to CRP in patients with diabetes mellitus
**P-value is statistically significant*
Pearson Chi-square value = 10.93; df = 4

DISCUSSION

CRP is a risk factor for ischemic heart diseases and diabetes mellitus[15]. It has been found that CRP was higher in subjects with diabetes than without diabetes[16]. It is still unclear that CRP in diabetes is related to glycemic status. Wu et al identified that CRP is directly proportional to HbA1c and proved statistically that HbA1c was 5.4% in subjects with low CRP and ≥7.5% in individuals with raised CRP. Former literature also observed the association between raised CRP and hyperglycemia[17].

In present study, the raised CRP was identified in 70 patients, of which 50(71%) subjects had raised HbA1c with female predominance. The present study also observed that raised HbA1c is significantly related to high CRP in subjects with

		CRP		Total	P-value
		Raised	Normal		
Gender	Male	30	5	35	
		42.9%	16.7%	35.0%	
	Female	40	25	65	0.01*
		57.1%	83.3%	65.0%	
Total		70	30	100	
		100.0%	100.0%	100.0%	

Table-III. The gender distribution in relation to crp in patients with diabetes mellitus
**P-value is statistically significant*
Pearson Chi-square value = 6.33; df = 1

		HBA1C		Total	P-value
		Raised	Normal		
Gender	Male	23	12	35	
		29.9%	52.2%	35.0%	
	Female	54	11	65	0.04*
		70.1%	47.8%	65.0%	
Total		77	23	100	
		100.0%	100.0%	100.0%	

Table-IV. The gender distribution in relation to hemoglobin a1c in patients with diabetes mellitus
**P-value is statistically significant*
Pearson Chi-square value = 3.87; df = 1

		HBA1C		Total	P-value
		Raised	Normal		
CRP	Raised	50	20	70	
		64.9%	87.0%	70.0%	
	Normal	27	3	30	0.04*
		35.1%	13.0%	30.0%	
Total		77	23	100	
		100.0%	100.0%	100.0%	

Table-V. The CRP and hemoglobin a1c in patients with diabetes mellitus
**P-value is statistically significant*
Pearson Chi-square value = 4.09; df = 1

diabetes. CRP has a role in the pathogenesis of type 2 diabetes and the development of insulin resistance[18]. A study published in 2013 also shown that CRP was higher in diabetic individuals with raised HbA1c than non diabetics[19]. The current series also found that the patients with established diabetes with raised HbA1c had frequently raised CRP as compared to the subjects with recent onset diabetes. Therefore it can be assumed that the information is not only responsible for the development of diabetes but also for persistent hyperglycemia in established diabetes.

Furthermore, the study published in 2005 observed that CRP is also a risk factor to develop diabetes mellitus later in acquired life,[20] whereas Festa, et al had found positive association between insulin resistance and C-reactive protein. The physiological mechanism of hyperglycemia in relation to CRP is inflammation, insulin resistance and endothelial dysfunction[21]. The inflammation also occurred due to oxidative stress on the endothelium and is augmented by hyperglycemia.[22] The female gender was predominance in our study and it is consistent with the study by Cottone S, et al[22].

We observed the positive correlation of systemic inflammation (raised CRP level) with type 2 diabetes regardless of obesity in our study population. Future advance studies are required to determine the association between genetic variations and CRP levels in subjects with type 2 diabetes mellitus.

CONCLUSIONS

It has been found that raised HbA1c is significantly related to elevation of CRP. Thus inflammation has a major influence on glycemic control in patients with diabetes. The advance research is needed to evaluate the important implications for diabetic subjects with raised CRP as far as management strategy is concerned.

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