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RELATIONSHIP BETWEEN C-REACTIVE PROTEIN AND GLYCEMIC INDEX IN TYPE 2 DIABETIC SUBJECTS

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Abstract:

Background & Objectives:-

Protein made by the liver C-reactive protein (CRP) is a well known indicator of systemic inflammation. Though it is taken to be non specific indicator of inflammation yet it is now considered to be an important risk factor for diabetes to develop. Therefore we carried out this study to evaluate the likely role of inflammation in Type 2 diabetics

Methodology: *After taking written informed consent, history taking and general physical examination of the 40 subjects was done who were registered in our study. We collected their fasting blood samples and sent to laboratory for fasting serum glucose, Insulin and CRP. HOMA IR model was used to assess the Insulin resistance. Data was presented as mean with standard deviation of every parameter of the current study. We used Pearson, s correlation test to decide relationship amongst C-reactive protein and glycemic index by noting fasting blood glucose and serum insulin levels. P value less than 0.05 was reflected statistically significant.*

Results: *Our study noted considerably greater levels of CRP, Fasting blood glucose, Insulin resistance, HOMA-IR and CRP amongst the diabetics. Positive correlation between CRP & HOMA-IR was exposed after Pearson's analysis*

Conclusion: *We concluded that a noteworthy association amongst insulin resistance and C - reactive protein in Type 2 diabetics.*

Key Words: *HOMA-IR, Inflammation, Diabetes mellitus, CRP*

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INTRODUCTION:

Diabetes Mellitus which is normally known as diabetes is a metabolic disease that leads to high blood sugar. It arises either if the pancreas does not yield sufficient Insulin or there is ineffective use of Insulin body produces. According to World Health Organization diabetes mellitus is well-known as a cluster of varied illnesses which display imperfect or scarce course of insulin secretion. Diabetes mellitus may show a inconstant degree of peripheral resistance of insulin which may lead to hyperglycemia with fasting blood glucose levels ≥ 126 mg/dl (1). As per survey conducted by World Health Organization people suffering from Type 2 diabetes has climbed to 422 million in 2014 from 108 million in 1980 (2). It was further explored that incidence of diabetes mellitus amongst grownups elder than 18 years has climbed from 4.7 % to 8.5 % with much speedy rise in middle & low income countries. It was noticed that diabetes was the straight cause of 1.6 million deaths in 2016 (2). By the year 2030, incidence of T2DM is further expected to increase to 522 million (1)

Type 2 diabetes is categorized by lessened secretion of insulin owing to weakening function of beta cells, compromised action of insulin, peripheral resistance of insulin and reduced hepatic glucose production (3). Pancreatic beta cells dysfunction and drop in mass of beta cells are reflected as the primary proceedings in the advancement of T2DM. In a study conducted by Lin & Sun it was observed that chronic hyperglycemia, oxidative stress, stress of endoplasmic reticulum, long standing hyperlipidemia and various inflammatory cytokines may lead to increased IRS-2 serine, threonine phosphorylation and degradation of proteasomes . It further leads to apoptosis of beta cells and reduction in cell mass (4)

C-reactive protein which is protein of acute phase is a delicate marker of systemic inflammation. Long standing inflammation of low-grade with high assembly of proteins of inflammation is thought to be associated in T2DM development (5). Raised high-sensitivity C-reactive protein is a potential reason of the etiology and manifestation of type 2 diabetes, even though the precise mechanisms are yet to be fully understood. C Reactive protein is documented to be a prime marker of inflammation linked with T2DM & its expression is regulated by Interleukin -6 & TNF Alpha (6)

Various cohort studies have documented the raised levels of CRP in male & female population labeling CRP a risk factor for T2DM development (7,8). The close association between CRP & T2DM isn't dependent on Insulin Resistance & Body Mass Index(7,9) Many studies declared the role of CRP in T2DM by noting that even after the BMI is adjusted for BMI, association amongst T2DM incidence & CRP remained statistically significant (7,10,11)

Qatanani and Lazar documented that adipocytes discharge Monocyte chemo attractant protein MCP-1, C reactive protein, Interleukin-6 (IL-6) and Tumor necrosis factor alpha (TNF α) which encourages inflammation and thus trigger our immune system therefore deregulating the pathway of insulin signaling (12) They noted raised levels of C-reactive protein, TNF Alpha & IL-6 in individuals who were obese and insulin resistant diabetics which resulted in development of T2DM. (12)

In another study conducted by Zhang and Zhang (2009), they found the association between lymphocytes, adipocytes and macrophages which may lead to progression of an inflammatory environment and further metabolic pathway deregulation.(13)

Continuous raised levels of CRP in patients of type 2 Diabetes Mellitus not only lead to onset of T2DM but it also increases the risk of developing complications (14). Our study aims to measure the levels of C-reactive protein and evaluate its association between C-reactive protein & Glycemic index in patients of T2DM

MATERIAL AND METHODS:

After taking approval from Ethical Committee of Postgraduate Medical Institute affiliated with Lahore General Hospital we enrolled forty male and female diabetic subjects at ages ranged between 35-55 yrs. Written informed consent was taken from the participants. We especially asked for diabetes duration in years, different health issues like ischemic heart disease, stroke hypertension, dyslipidemia, infection and various endocrinological disorders. We also asked about the use of drugs which modify serum CRP blood including cholesterol lowering drugs thiazolidinedione, phenytoin, corticosteroid and hormone replacement therapy.

Subjects enrolled in the study were also probed about any history of alcohol intake and use of cigarettes. All subjects undertook general physical examination. 5ml blood sample was taken & sent to laboratory. Glucose was estimated the same day of blood collection while serum was centrifuged and kept in serum vials at minus 800C for further use.
Kit of Fortress Diagnostic was used to estimate plasma glucose by glucose oxidase technique while

kit of Bio Source was used to assess Human Insulin by solid stage enzyme amplified sensitivity immunoassay .We determined C-reactive protein by using kit of Abazyme

We determined mean and standard deviation of each parameter of our study was determined. We used Pearson's correlation test to assess the correlation between fasting blood glucose, insulin HOMA-IR and C-reactive protein. P value less than 0.05 was reflected significant statistically. We used SPSS version 16 for our data analyses

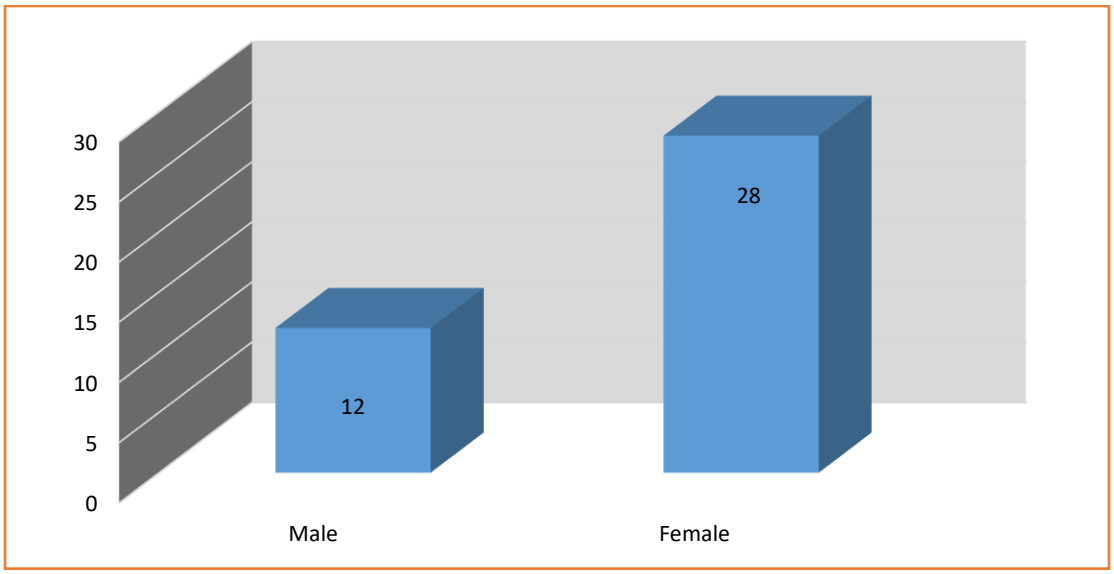
RESULTS:

40 diabetic subjects (mean ± SD 43.97 ± 6.581) which included 28 females (mean ± SD 44.54 ± 6.39) and 12 males (mean ± SD 42.67 ± 7.01) were included in this study. We found significant difference between age of males & female patients on bivariate analysis (p = 0.48)

Fasting blood glucose was significantly greater (p = 0.000) in diabetics 164 ± 46 mg/dl) than in controls (83 ± 8 mg/dl). Likewise, serum insulin was significantly greater (p = 0.000) in diabetic subjects (37 ±7 µU/ml) than in non diabetic subjects (26 ± 6µU/ml). Additionally HOMA-IR values showed that T2DM subjects had a highly significant increase (p = 0.000) in resistance of insulin (19 ± 8) as matched with normal subjects.

Pearson's correlation test were used to assess correlation between fasting blood glucose, serum insulin, insulin resistance and C-reactive protein. A significant +ve correlation was found between serum CRP, HOMA-IR and BMI (r = 0.509, p = 0.001), HOMA-IR (p = 0.561, r = 0.000) and CRP (r = 0.617, p = 0.000) in diabetic subjects. We also found a strong relationship amongst CRP and HOMA-IR, the correlation coefficient is found 0.478 was the correlation coefficient with p-value of 0.002

Demographic data of study population

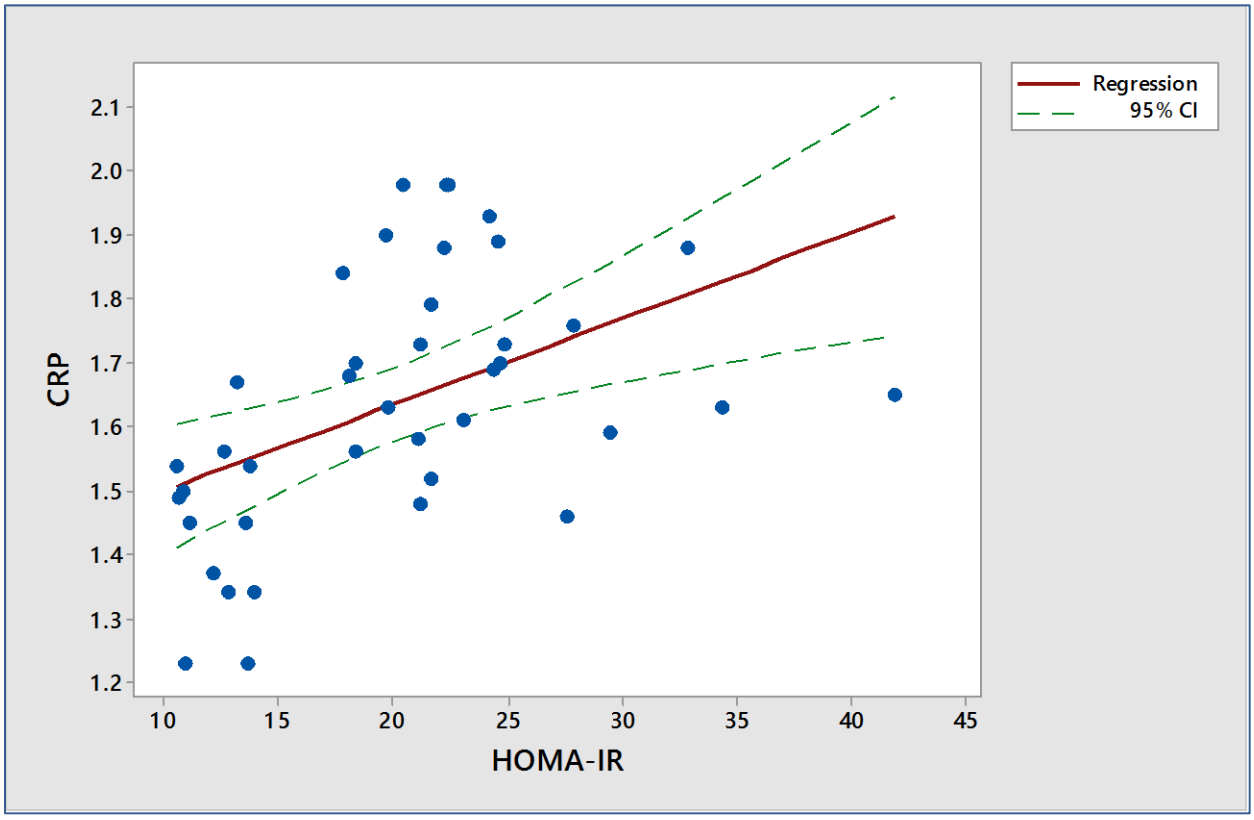


Parameter	For All (40) Mean ± SD	Male (12) Mean ± SD	Female (28) Mean ± SD	P-value
Age	43.97±6.581	42.67± 7.101	44.54 ± 6.39	0.48
HOMA-IR	20.17±7.15	19.73± 7.12	20.36± 7.29	0.55
CRP	1.63±0.20	1.66±0.20	1.62±0.038	0.82

Glycemic parameters in the diabetic male and female groups

Variables	**For all(40) Diabetics**	**Male n= 12 Mean ±SD**	**Female n=28 Mean ± SD**	**P value**
Age	**43.97 ± 6.581**	**42.67 ± 7.12**	**44.54 ± 6.39**	**0.48**
Blood sugar fasting mg/dl	168 ±0.81	164 ± 46	168 ± 08	0.045
Insulin IU /ml	39± 48	37 ±1 7	39 ±16	0.01
HOMA-IR	20.17 7.15	19.73 7.12	20.36 7.29	0.55
CRP	1.63 0.20	1.66 0.20	1.62 0.038	0.82

Relationship between CRP and HOMA -IR



DISCUSSION:

Our study equated the levels of CRP in Type 2 diabetics and evaluated the relationship amongst CRP and existence of compromised glycemic control. It is well documented that chronic inflammation has a leading role in the development of T2DM. Bases of inflammatory cytokines that control inflammatory responses in these patients are immune cells, triggered by hyperglycemia and associated metabolic illnesses. In a study done by Qatanani and Lazar it was noted that higher concentration of C-reactive protein were found in the patients who were insulin resistant which finally resulted in the progress of T2DM

This study also proved that a higher HOMA - IR is meaningfully associated with a larger possibility of higher CRP among adults having diabetes. This relationship was statistically significant when CRP and HOMA - IR level were compared and further evaluated in logistic regression models to foresee raise in the levels of CRP after adjusting for age, gender, race, BMI, smoking, level of insulin and diabetes duration[15]

Numerous studies have proposed that inflammation is closely associated with insulin resistance which has an important calculative role in pathogenesis of T2DM [16, 17]. Besides close association of IR with T2DM, hyperglycemia may encourage the process of inflammation which may accelerate the development of DM [18]

As our study is a cross sectional study so in this study we cannot conclude a cause and effect relationship. We cannot predict if weak glycemic control has a decisive role in inflammation or inflammation itself leads to raised glucose levels. It is possible that a third factor may influence both. EricBrunner et al witnessed that associations between serum CRP and insulin resistance, glycaemia and diabetes may be non causal. Though prospective studies are desired to explore the causal relationship yet any causality direction will have significant inferences [19]

If inflammation is triggered by poor glycemic control, then improved glycemic control should lower inflammation and hence lower the threat of diabetes. Latest research supports a connection between inflammation and hyperglycemia. Similarly important association between insulin resistance and CRP was found in different racial inhabitants like Japan, Americans, Africans and Indians [20, 21, 22, 23]. These results are in matching with the conclusions of the current study, which further tells the association

amongst inflammation and hyperglycemia in diabetic adults

Results of our study offer added support for a relation between glycemic control and systemic inflammation in recognized diabetics. Future studies should be conducted to assess the direction of this association; so that it would have better inferences for the treatment of adult diabetics

We had certain limitations in our study. We could not establish a definitive causal relationship between Insulin resistance & C reactive protein as our study was a cross sectional study. Our sample size was small and we could not explore the important role of other cytokines related to inflammation

CONCLUSION:

This study elaborated the fact that weak or poor glycemic control is significantly associated with diabetes development. It specifies that C-reactive protein is a key risk factor for diabetes.. Additional studies should evaluate the actual role of inflammation in diabetes so as to avoid the danger of developing diabetes mellitus.

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