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Original Research Paper

COMPARISON OF FASTING BLOOD GLUCOSE AND C-REACTIVE PROTEIN LEVELS BETWEEN FIRST DEGREE RELATIVES OF TYPE 2 DIABETIC PATIENTS WITH IHD AND WITHOUT IHD-CRP AS AN INDEPENDENT MARKER FOR IHD

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ABSTRACT:

Background:-CRP is an important inflammatory marker in the pathogenesis of metabolic disorders. One of the major complications in diabetes mellitus patients is cardiovascular disease. CRP may help to predict among Pre-diabetic patients are at higher risk for Ischemic heart disease (IHD). Several cumulative studies indicate that CRP levels are altered in individuals with a family history of diabetes. The aim of this study was to explore the comparison and association of CRP levels between the first degree relatives of type-2 diabetes with IHD and without IHD patients. **Material and method:-** The present study access fasting Blood glucose levels and inflammatory marker CRP in two groups. Group A comprised 50 first degree relatives of type 2 diabetes with IHD and Group B consist of 50 first degree relatives of type 2 diabetes without IHD. **Result:-**The mean of CRP and Fasting Blood Sugar were significantly ($p<0.05$) higher in 1st degree relative to type 2 diabetic patients with IHD. It also seems to be slightly elevated levels of CRP in 1st degree relatives of type 2 diabetics without IHD. **Conclusion:-** The study has shown that CRP is an independent marker in early diagnosis of IHD in 1st degree relatives of type 2 diabetics. It has also been seen that strong family history of type 2 diabetic patients who are in Pre-diabetic stage has shown slightly increased level of CRP and patients have fasting sugar level is within the normal range when we compare the two parameters FBS and CRP in pre-diabetics patients. So, we can use CRP as an important diagnostic tool for the prevention of IHD in those patients who have a family history of diabetes.

Keywords:- Hyperglycemia, C-Reactive Protein, Ischemic Heart Disease, Diabetes Mellitus, Pre-diabetics

INTRODUCTION:-

Once regarded as a single disease entity, diabetes is now seen as a heterogeneous group of diseases, characterized by a state of chronic hyperglycemia and also leads to major complications like obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease in the future[1]. By the year 2025[2] prevalence of diabetes is higher in developed nations than in developing nations. There is a strong association between the development of type 2 diabetes with a family history of the disease, 74% to 100% of patients have a first or second-degree relative with diabetes mellitus[3]. Patients are at higher risk for both type 2 diabetes mellitus[4] and ischemic heart disease which are having a positive

family history. CRP is an important inflammatory marker in the pathogenesis of this metabolic disorders[5]. Recently a study has postulated to be the association between CRP and metabolic syndrome pointed to the direct harmful effect of CRP on vessel walls which may alter endothelial permeability and eventually lead to insulin resistance6.CRP is produced by hepatocytes and its gene expression is regulated by inflammatory cytokines such as interleukin 6 (IL-6) and TNF-α,7. Among several markers of systemic inflammation, CRP shows the strongest associations with vascular events, and the addition of CRP to total cholesterol dramatically improves risk prediction8. CRP is not only a parameter that shows the severity of inflammation in metabolic disorders, moreover, it is also a causative factor that induces endothelial damage itself9. The inflammatory mediators like IL6, and CRP are responsible to decrease the tissue sensitivity to insulin[10] Finally, in our observation of the elevated levels of CRP seen in the family history of type 2 diabetic patients, it may be used as a diagnostic or prognostic marker for the prevention of ischemic heart disease in the future. Acknowledging all these challenges, our present study aimed to identify the role of CRP in what extent of Pre-diabetes in first degree relatives of T2DM patients and to assess their future cardiovascular risk.

MATERIAL AND METHODS:-

The current study was undertaken in Biochemistry, in collaboration with the medicine department, Government Medical College, Amritsar. A comparative study was conducted among OPD and IPD patients of the medicine department. We divided all patients into two groups. Group A consists of 50 first degree relatives of diabetes mellitus with IHD and compare with group B 50 family history of diabetics without IHD patients. The criteria to diagnose Diabetes mellitus is on the basis of WHO strategy. All the patients were undergoing fasting blood glucose and fasting CRP tests as well as routine investigations like lipid profile and ECG. The study was conducted after taking ethical approval from the institutional ethical committee. Written consent was taken from all study participants.

Inclusion criteria:- Diabetes mellitus, and cardiovascular disease patients were included.

Exclusion criteria:-The patients suffering from cancer, liver disease, kidney disease, and thyroid disease were excluded from the study.

5 ml of venous blood was taken with a dry disposable syringe under aseptic conditions by vein puncture in the antecubital vein in a disposal vial for biochemical analysis of FBS, Total Cholesterol (TC), Triacylglycerol (TG), LDL, VLDL, HDL, and CRP. FBS and Lipid profiles were estimated by enzymatic method on semi auto-analyzer. Serum fasting C-Reactive Protein estimation- By Latex Method [11]. It semi-quantitative time technique. The CRP reagent contains Latex particles coated with an Anti-Human CRP antibody. When the reagent is mixed with serum containing CRP at a level greater than 5mg/dl, the particles agglutinate. This is interpreted as being a positive sample. Analysis of data was done on spss version 15. Data were expressed as mean SD. Student t was applied to compare variables between groups. The Pearson correlation coefficient values were used to detect the association among different variables.

DISCUSSION:-

In the last decades, there is an increased incidence of, diabetes mellitus an individual is more in the presence of family history. In the Indian population, 75% of Diabetic patients have first degree family history of diabetes[12]. The activation of the immune system and chronic inflammation act as an important factor in the pathogenesis of many diseases, also include metabolic disorders. [13]. C-reactive protein (CRP), a marker of systemic inflammation, is emerging as an independent risk factor for cardiovascular disease[14,15,16]. CRP noncovalently bound disc-shaped pentamer. It is consisting of five identical subunits[17]. Each subunit consists of 206 amino acids and it carries 2 calcium ions for the pentameric[18]. It is an acute phase reactant and produced in hepatocytes as a pentamer structure of identical subunits in response to cytokine s[19]. Based on so many interventional and epidemiological studies, increased levels of CRP are associated with cardiovascular risk in futue[20]. The most prevalent cause of mortality or morbidity among diabetic populations is cardiovascular disease[21]. Account for virtually, the death rates are 1.7 times higher in diabetics adults due to cardiovascular disease in the world[22,23] The present study was conducted on 50 patients with a family history of type 2 diabetes without IHD and 50 patients with a family history of diabetes with IHD. The aim of the study was to find out the comparison and correlation between CRP and FBS among prediabetics and diabetics

patients with and without IHD. Our study has shown a significant role of CRP in prediabetic patients without IHD. As results were compared and suggested that CRP levels are slightly increased in patients with a family history of diabetes but not from cardiovascular disease. Moreover, the 1st degree relatives of the diabetic patients with IHD were seen highly increased CRP levels. In addition recent studies, suggests that patients with elevated levels of CRP are at higher risk of diabetes[24,25] hypertension and cardiovascular disease. Hyperglycemia and Chronic systemic inflammation, further leads to chances of the development and progression of atherosclerotic cardiovascular disease. Many observational studies have confirmed the inter-relationship between CRP, hyperglycemia, and atherosclerosis[26,27,] It has also been seen that in the case of elevated levels of CRP, hyperglycemia exaggerates the pro-atherogenic effects of CRP[28]. Moreover few studies have concluded that the correlation between CRP levels and the level of glycemic status showed conflicting results. In addition, some studies had proven the positive co-relation between glycemic control and CRP levels[29,30,31]. Many past observation studies have confirmed that patients with type 2 diabetes are especially at risk for the development of macroangiopathy[32]. Several studies have reported a significant positive association between elevation in CRP levels and the future risk of diabetes even after adjustment of BMI[33] All previous studies have concluded that CRP is an early diagnostic marker in first degree relatives in type 2 diabetic patient and is also helpful in the diagnosis of early risk factors in cardiovascular disease in these patients. We also observed that positive family history of type 2 diabetics has increased the risk of type 2 diabetes mellitus and ischemic heart disease. It seems that CRP levels slightly increase in prediabetics patients. Thus the risk of IHD in prediabetics can be reduced by improving glycemic control.

RESULT:-

The study was conducted with a sample size of 50 first degree relatives of diabetes mellitus with IHD and 50 first degree relatives of diabetes mellitus patients without IHD. The majority of patients are above 30 years. The aim of this study was to explore the comparison and correlation of CRP levels between the first degree relatives of type-2 diabetes with IHD and without IHD patients. The results observed in the present study from both groups were as follow:-

Group A:-Ist degree relatives of type 2 diabetes mellitus with IHD

Group B:-Ist degree relatives of type 2 diabetes mellitus without IHD

Table No.-1. Comparison of FBS and CRP in first degree relatives of type-2 diabetics with IHD (group A) according to fasting blood glucose levels

Sr. No.	No. Of cases	FBS Range	FBS Mean ± SD	CRP Mean ± SD	P Value
1.	10	< 100 mg/dl	89.5± 5.49	5.68 ± 0.19	0.47
2.	15	100-125 mg/dl	116.3± 6.42	8.19 ± 0.39	0.19
3.	25	>126 mg/dl	139.7±12.7	9.75± 1.22	0.016

FBS Range:- Non-Diabetic(<100mg/dl), Pre-Diabetic(100-125mg/dl), Diabetic(>126mg/dl)

Table No. 1 depicts that the first degree relatives of type 2 patients with IHD were distributed into three groups on the basis of fasting blood glucose levels 100 mg/dl, 100-125 mg/dl and 126 mg/dl respectively . Group I (n=10) having FBS < 100 mg /dl with mean ±SD 89.5± 5.49 and CRP levels with Mean± SD 5.68± 0.19, (P< value 0.47) Group II. (n=15) having FBS 100 -125mg /dl with mean ±SD 116.3±6.42 and CRP levels with Mean±SD 8.19±0.39,(P<0.19). Group III(n=25) having FBS >126mg /dl with mean ±SD 139.7±12.7 , and CRP levels with Mean±SD 9.75±1.22,(P<0.016).

Table no:- 2. Comparison of FBS and CRP in first degree relatives of type-2 diabetics without IHD (Group B) according to fasting blood glucose levels

Sr. No.	No. of cases	FBS Range	FBS Mean±SD	CRP Mean± SD	P> value
1.	10	< 100 mg/dl	81.6 ± 6.19	4.69 ± 0.57	0.53
2.	15	100-125 mg/dl	112.4 ± 6.02	7.89 ± 0.79	0.34
3.	25	>126 mg/dl	134.04 ± 5.28	8.27 ± 0.49	0.027

FBS Range:- Non-Diabetic(<100mg/dl), Pre-Diabetic(100-125mg/dl), Diabetic(>126mg/dl)

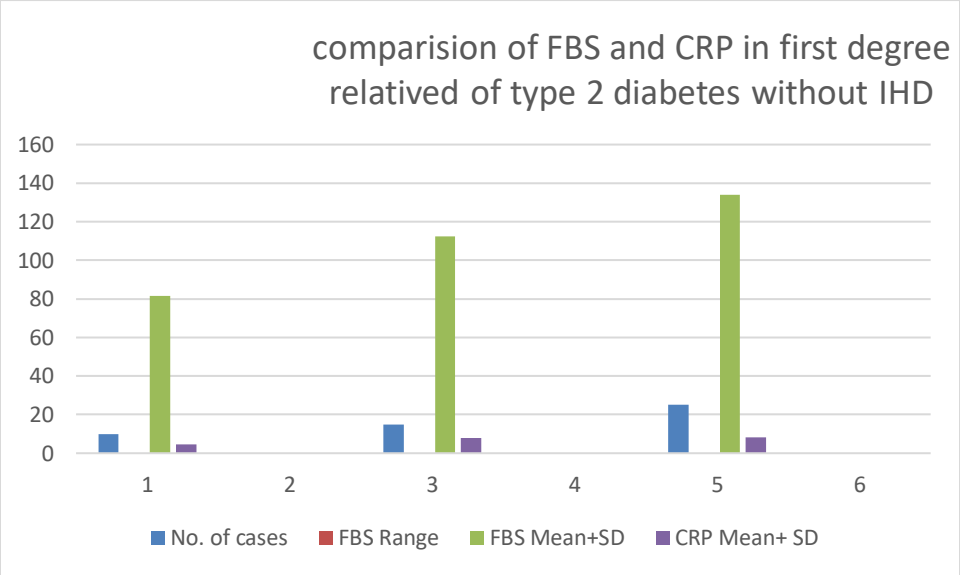

Table No. 2 depicts that the first degree relatives of type 2 patients without IHD were distributed into three groups on the basis of fasting blood glucose levels 100 mg/dl, 100-125 mg/dl and 126 mg/dl respectively . Group I (n=10) having FBS < 100 mg /dl with mean ±SD 81.6 ± 6.19 P and CRP levels with Mean± SD 4.69 ± 0.57(P <value 0.53). Group II. (n=15) having FBS 100 -125mg /dl with mean ±SD 112.4±6.02 and CRP levels with Mean±SD 7.89±0.79(P< 0.34). Group III(n=25) having FBS >126mg /dl with mean ±SD 134.04±5.28 and CRP levels with Mean±SD 8.27±0.49(P< 0.027).

Table No- 3. FBS and CRP levels in between two Groups -Group A and Group B

Sr. No.	FBS Range	Group A	Group A	Group B	Group B
		FBS Mean ± SD	CRP Mean± SD	FBS Mean± SD	CRP Mean± SD
1.	< 100 mg/dl	89.5± 5.49	5.68±0.19	81.6 ± 6.19	4.69 ± 0.57
2.	100-125 mg/dl	116.3± 6.42	8.19±0.39	112.4 ± 6.02	7.89 ± 0.79
3.	>126 mg/dl	139.7±12.7	9.75±1.22	134.04 ±5.28	8.27 ± 0.49

FBS Range:- Non-Diabetic(<100mg/dl), Pre-Diabetic(100-125mg/dl), Diabetic(>125mg/dl)

Table No. 3 shows the comparison between two groups A and B on the basis of parameters FBS and CRP. Thus it depicts that serum C- reactive protein levels were seen slightly increase in prediabetic patients whose FBS levels were with in range. So, it shows the significant role of CRP in first degree relatives of type 2 diabetes.

In our study, it is observed by the fact that inflammation by CRP, is an independent and strong early indicator of IHD in first degree relatives of type 2 diabetes mellitus.

CONCLUSION:-

Hence, We conclude that in patients with a strong family history of type 2 diabetes, low grade inflammation is reflected by increased plasma levels of inflammatory biomarkers such as C-reactive protein (CRP). Slightly increases in CRP predict the likelihood of developing ischemic heart disease events in a family history of type 2 diabetics populations. In addition, in apparently healthy subjects with strong family history, increased levels of CRP have been shown it's a predictive role in determining cardiovascular risk, and may represent an active participant in atherogenesis. Taking into account the above facts it can be said that early identification and efforts to improve glycemia in persons with prediabetes have the potential to reduce or delay the progression of diabetes and related cardiovascular diseases. Our study establishes a strong correlation between CRP and fasting blood glucose in prediabetics patients with IHD and without IHD and is also used as a diagnostic tool for screening among patients to prevent the development of IHD in the future.

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