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Original Research Article

Association of c-reactive protein and lipid accumulation product with fasting insulin levels in obese first degree relatives of type-2 diabetics

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ABSTRACT

The obese first degree relatives of type 2 diabetics are more prone to develop diabetes mellitus in later life. Having one parent with type 2 diabetes mellitus carries 1.6 fold and both the parents with type 2 diabetes mellitus (T2DM) has 3.2 fold higher risk of developing T2DM. Lipid accumulation product (LAP) is a simple and reliable index of central lipid accumulation. It combines waist circumference and triacyglycerols. Studies have revealed that LAP is a better indicator than Body mass index (BMI) in predicting risk of diabetes mellitus and metabolic syndrome. Weight gain and body mass are the main factors in increasing risk for diabetes mellitus. Fat cells produce chemicals (inflammatory markers) that cause inflammation. Internal inflammation can also leads to the development of diabetes mellitus. C - reactive protein (CRP) is an inflammatory marker produced by liver cells. Studies have shown that elevated CRP is linked to higher risk of developing diabetes in later life. In this study, we have found an association of Serum Insulin (SI), LAP and CRP in first degree relatives of type-2 diabetics. We had taken 100 Obese first degree relatives of type-2 diabetics as subjects and 100 age and sex matched first degree relative of T2DM without obesity were taken as controls. Fasting blood glucose, Fasting TGs estimations were done using fully autoanalyser. Waist circumference (in cm) was measured and also LAP score was calculated by using the formula, i.e. (WC-58)*TG mmol/l & (WC-65)*TG mmol/l in females and males respectively. CRP was estimated using Nyco-card reader. Serum Insulin was measured using ELISA reader. The Mean ±SD of Serum Insulin, CRP, LAP, FBS in Group I were found to be 15.9±2.54, 6.05±1.5mg%, 106.8±40.7, 133.0±18.9 mg% respectively compared to Group II 9.2±1.28, 2.59±1.2, 25.7±14.6, 78.7±8.2. A highly significant correlation of LAP and CRP ($p<0.01$) was found in study group. A significant correlation of Serum Insulin (SI), CRP and LAP score ($p<0.5$) was found. This study suggested that first degree relatives of type-2 diabetics should have some modification in their lifestyle as they are at increased risk of metabolic syndrome, diabetes and coronary artery disease.

1. Introduction

The prediction that over 366 million people worldwide will suffer from Type 2 Diabetes Mellitus (DM) by 2030 has become a worldwide concern.[1] It is a multifactorial disease presenting with chronic hyperglycemia. The metabolic derangements occur sometimes before onset of diabetes. Through unresolved mechanisms, genetic predisposition, ethnicity, changes in BMI, lipid profile are contributing to its pathogenesis.[2] Growing evidences have shown that the first degree relatives (FDR) of patients with T2DM are more susceptible to develop insulin resistance and defects in insulin secretion.[3] FDR can be described as having a parent, sibling or child with T2DM. There is a strong connection between BMI, Lipids (TGs and TCs) and diabetes in FDR of T2DM.[4] It is accepted that

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dyslipidemia, raised TGs and TCs affect β- cell function in diabetes mellitus.[5] Prolonged TGs exposure leads to a chronic phase associated with loss of β-cell function and impaired glucose tolerance.[6] LAP an index of central lipid adiposity has been proposed as a reliable risk indicator of insulin resistance, metabolic syndrome, cardiovascular diseases and diabetes mellitus.[7–9] It also has a relation with visceral adiposity.[10] The use of TG levels in combination with waist circumference termed as hyper triglyceridemic waist is able to find individuals with highest amount of visceral fat.[11] The higher LAP in healthy individuals is associated with abnormal glucose homeostasis and insulin resistance.[12] It is established that obesity and increased visceral adipocytes contribute to increased levels of several inflammatory proteins such as CRP, IL-6, and PAI.[13] Underlying low grade inflammation with raised production of proteins associated with inflammation leads to T2DM.[14] CRP levels are regulated by interleukin-6 and TNF - *a* produced by adipocytes.[15] The mechanism of association between CRP and T2DM is not clear. Some factors like oxidative stress can also lead to low grade inflammation[16] and genetic predisposition might lead to T2DM. Elevated CRP might induce insulin resistance by increasing thrombogenic agents, stimulating complement cascade, increasing expression of endothelial adhesion molecules (EAM).[17,18]

2. Aims and Objectives

The present study was aimed to find association of CRP and LAP with Fasting Insulin levels in obese first degree relatives of type 2 diabetics.

3. Materials and Methods

3.1. Study population

The study was performed in Department of Biochemistry in Guru Gobind Singh Medical College and Hospital, Faridkot. Data was collected through questionnaires. Inclusion criteria for study participation included: 1) First degree relatives of patients with Type 2 Diabetes Mellitus aged 30 to 70 years having simple obesity through physical examination (2) BMI greater than 25 kg/m^2 for obese; (3) participants must have stable body weight for at least three months prior to study (4) no weight loss by taking any dietary plans.

Based on the above criteria, 100 obese first degree relatives of type 2 diabetics were selected to participate in the study. Informed consent was taken. 100 age and sex matched first degree relative of T2DM without obesity were taken as controls.

3.2. Anthropometric measurements

The height was measured with wall mounted stadiometer. Weight was also assessed using a weighing machine. Body mass index (BMI) was calculated using the weight and height measurements. Waist circumference measurements were taken at the mid-point between the bottom rib and the hip bone.

3.3. Lab data

Overall 10 hr fasting sample was taken to measure blood glucose, triglycerides and Fasting insulin. Blood glucose was measured by using fully auto analyser. Serum LDL cholesterol was calculated using Friedewald's equation, except for triglycerides > 400 mg/dL. Moreover, Serum insulin was determined using an enzyme-linked immunosorbent assay (ELISA). The sensitivity of the assay was 1.5 μU/ml and the coefficient variation for inter-assay and intra-assay were 6.29 and 7.67% respectively. CRP was measured using Nyco card reader. LAP was measured using formula: (WC-58)*TG mmol/l & (WC-65)*TG mmol/l in females and males respectively.

Statistical analysis was performed using SPSS.

3.4. Cut off values

Serum Insulin >12μIU/L was considered as insulin resistant. Normal value of Insulin is upto <9μIU/L. C-reactive protein of 5 mg% were considered as normal. LAP cut off values in our population (cm·mmol/L) for males were, 65.8 and 103.4 (range: 21.6–247.9); females, 44.7 and 81.5 (range: 11.6–215.4).

4. Results

In the study population, the mean fasting blood glucose was higher than the control group. The average values of most of the parameters were higher in study group I. (Table 1)

Table 1: Showing basic characteristics of both the groups

Characteristics	Group I Mean ±SD	Group II Mean ±SD
Fasting Blood Glucose	133.0±18.9	78.7±8.2
BMI (kg/m2)	27.09±10.62	21.29±2.44
Total cholesterol (mg/dL)	220.2±6.6	150.2±8.6
LDL cholesterol (mg/dL)	147.2±7.2	128.2±9.6
Fasting insulin (U/L))	15.9±2.54	9.2±1.28
C Reactive Protein	6.05±1.5	2.59±1.2
LAP	106.8±40.7	25.7±14.6

A highly significant correlation of LAP and CRP ($p<0.01$) was found in study group. A significant correlation

of Serum Insulin (SI), CRP and LAP score with FBS ($p<0.05$) was found. Also, Figures 1, 2 and 3 shows the correlations between LAP, CRP and Insulin. Overall this present study, suggested that obese FDR of T2DM shows more insulin resistance and inflammation which can further be the underlying factor predisposing to it.

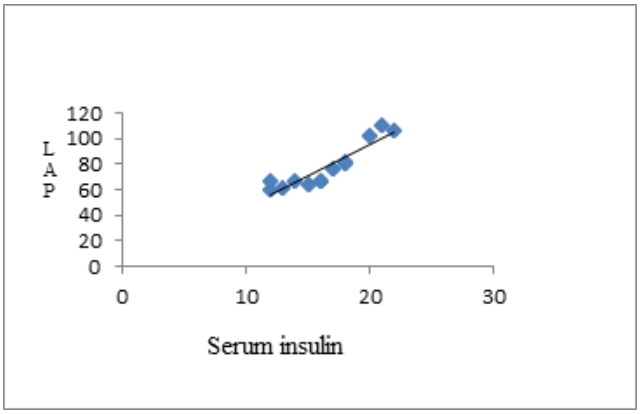

Fig. 1: Correlation between LAP and Insulin in FDR T2DM

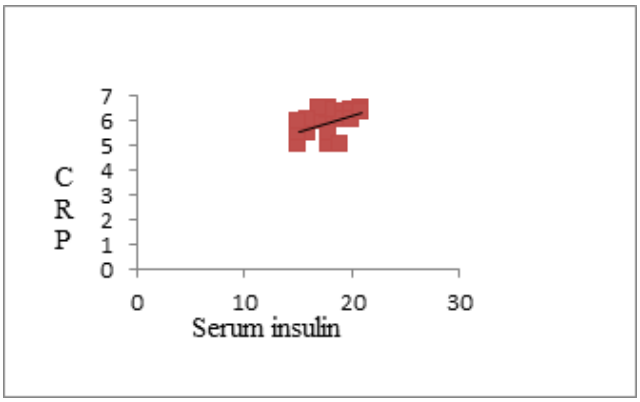

Fig. 2: Correlation between CRP and Insulin in FDR of Type2 DM

5. Discussion

In the present study, we have chosen FDR of T2DM as they are at increased risk of developing T2DM due to genetic predisposition and obesity. We have showed the association of LAP and CRP with fasting insulin and blood glucose levels in obese first degree relatives of type-2 diabetics. LAP and CRP are reliable predictors of risk of diabetes. They have shown a correlation with insulin resistance.

In the current study, LAP index was related to higher fasting insulin and blood glucose values showing insulin resistance in FDR T2DM group. Our results are supported by some studies. Kan Sun et al. has recently found relatively strongest association of LAP than other adiposity parameters with increased measures of Insulin resistance and diabetes mellitus. A strong association of LAP with

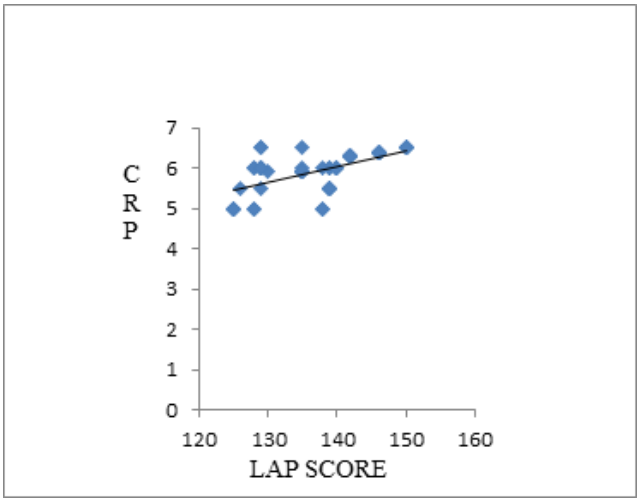

Fig. 3: Correlation of CRP and LAP in FDR of Type 2 DM

fasting plasma glucose, glycosylated hemoglobin and fasting insulin was also found.[19] Moreover another study found that obese FDR of T2DM with elevated triglycerides (a component of LAP) levels had HOMA 2-IR score indicating some degree of insulin resistance.[2]

We examined the relationship between CRP, Fasting insulin and found more insulin levels than non obese FDR of T2DM. Suganya et al[20] found an association of CRP concentrations with increased risk of developing T2DM. Various other recent studies are supporting association of CRP with risk of developing diabetes mellitus.[21–23] Another study had revealed that increase in CRP is strongly associated with risk of type-2 diabetes compared with subjects with a low level among both men ($P = 0.028$) and women ($P = 0.004$).[24] CRP plasma levels were significantly higher in subjects with family history than subjects without family history. Moreover, they found an independent association of CRP with age, family history, body mass index, waist circumference, and $HOMA_{IR}$.[25]

A correlation between LAP and CRP was also found confirming the fact that adipocyte produce inflammatory proteins such as CRP, IL-6, P-selectin contributing to underlying inflammation that may be a contributor to insulin resistance. The markers are unique in sense because both the markers are easy to perform. LAP combines Waist circumference and TG levels. Due to stability in plasma and serum, estabilished standards have made CRP, a reliable marker of inflammation. We used fasting Insulin for assessing risk of insulin resistance in obese people. Another study suggested that fasting insulin (FI) is sensitive and reliable marker in detecting Insulin resistance in obese. So, FI can be used as an easy test to detect IR in obese people.[26] The present study has some limitations such as small sample size. So, further studies with more sample size should be done to establish association of LAP and CRP with risk of

developing diabetes in FDR of T2DM.

6. Conclusion

LAP and CRP has shown to be reliable indicators of incidence of diabetes in FDR T2DM. These simple tests may help in clinical settings to identify individuals at increased risk of T2DM.

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflict of interest.

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