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A study to observe levels of inflammatory markers and their correlation with dyslipidemia in diabetics

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ABSTRACT

The present study was undertaken to observe levels of inflammatory markers and their correlation with dyslipidemia in diabetics. 35 diabetic patients, already diagnosed and attending diabetic clinic and 35 normal healthy subjects aged 30-70 years were recruited for the present study by convenient sampling technique. Fasting serum sample was taken for analysis of plasma glucose, glycated haemoglobin (HbA1c), serum total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, serum CRP, serum Cp, serum TSA. Data were analysed using Microsoft excel. We conclude that, a strong association was present between inflammatory marker TSA and lipid profile. This study revealed that low grade inflammation is found in diabetic patients. The coexistence of metabolic syndrome and proatherogenic profile in T2DM needs urgent intervention as these can lead to future cardiovascular problems.

Keywords: C-reactive protein (CRP), Ceruloplasmin (Cp), Dyslipidemia, Glycated haemoglobin (HbA1c), Inflammatory markers, Type II Diabetes(T2DM), Total sialic acid(TSA).

INTRODUCTION

Diabetes is a metabolic disease, which occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces. This leads to an increased concentration of glucose in the blood (hyperglycemia) [1]. A total of 347 million people worldwide have diabetes. In 2004, an estimated 3.4 million people died from consequences of fasting high blood sugar. A similar number of deaths have been estimated for 2010. More than 80% of diabetes deaths occur in low- and middle-income countries [2-5]. India is having a second largest number of subjects with diabetes [6-8]. Indian population is more likely to develop Type 2 diabetes due to changes in their lifestyle toward deleterious pattern, and this transition is more rapid in Kerala [9]. Simple lifestyle measures have been shown to be effective in preventing the onset of Type 2 diabetes [10]. Type 2 diabetes is an inflammatory atherothrombotic condition associated with a high prevalence of cardiovascular disease. In patients with type 2 diabetes, low grade inflammation is reflected by increased plasma levels of several biomarkers of inflammation such as C-reactive protein (CRP). Small increases in CRP predict the likelihood of developing cardiovascular events both in diabetic and nondiabetic populations. In addition, in apparently healthy subjects, increased levels of CRP predict the risk of developing type 2 diabetes [11]. In addition, Serum L-fructose, total sialic acid and ceruloplasmin

can also be used as prognostic indicators for type II diabetes mellitus [12]. It was reported that low-grade inflammation exists in Diabetes mellitus and it is positively related with dyslipidemia (except for HDL cholesterol) in diabetics [13]. The present study was undertaken to observe levels of inflammatory markers and their correlation with dyslipidemia in diabetics.

MATERIALS AND METHODS

The study was approved by Institutional Ethics Committee. A written, informed consent was obtained from all the participants. The study was performed in accordance with the "Ethical Guidelines for Biomedical Research on Human Participants, 2006" by the Indian Council of Medical Research and the Declaration of Helsinki, 2008.

Participants, inclusion and exclusion criteria

35 diabetic patients, already diagnosed and attending diabetic clinic and 35 normal healthy subjects aged 30-70 years were recruited for the present study by convenient sampling technique. The following criteria were used to recruit the patients.

Inclusion criteria

1. Diabetic patients already diagnosed and attending diabetic clinic
2. Willing participants

Exclusion criteria

1. Pregnant women,
2. Age below 30 years
3. Diabetics with complications

METHODS

Fasting serum sample was taken for analysis of plasma glucose, glycated haemoglobin (HbA1c), serum total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, serum CRP, serum Cp, serum TSA .Glucose was measured by glucose oxidase-peroxidase method and HbA1c by cation exchange resin method. Commercial enzymatic methods were used in determination of total cholesterol, HDL cholesterol and Triglycerides. LDL cholesterol was estimated using Friedewald equation (Friedwald et al). Turbidimetric immunoassay method was used for CRP estimation, Ceruloplasmin by copper oxidase method, and TSA by thiobarbituric acid method respectively [14-20].

Data analysis

Data were analysed using Microsoft excel. Student't' test was used to determine significance of difference between cases and controls. Pearson's correlation coefficient was used to determine the correlation between the variables. P value <0.05 is considered statistically significant.

RESULTS

Results are presented in table no 1 to table no3. Mean BMI, systolic BP, Diastolic BP were significantly elevated in cases than controls. T2DM patients had significantly elevated Total cholesterol, TG, LDL cholesterol while HDL cholesterol is significantly decreased compared to healthy controls. Mean LDL/HDL ratio is found to be elevated in diabetic patients. All these are components of metabolic syndrome. Inflammatory markers CRP, Cp and TSA were significantly elevated in T2DM compared to controls. HbA1c and FBS were also significantly elevated in T2DM when compared to controls. Strong positive correlation was present between TSA and LDL (P=0.011), TSA and TG (P=0.003), TSA and Total cholesterol (P=0.005).A negative but insignificant correlation is found between TSA and HDL. No significant correlation was observed between inflammatory markers and glycemic profile.

Table 1: Main characteristics of cases and controls

Variable	Controls (35)	Cases(35)	P value
Age	44.37±10.33	54.89±7.18	0.0001
BMI	28.53±2.31	31.23±2.39	0.0001
SBP	136.23±10.424	152±15.02	0.0001
DBP	85.54±5.089	92.34±6.33	0.0001
CRP	1.07±0.56	3.71±1.49	0.0001
TSA	64.35±7.29	87.25±13.65	0.0001

Cp	27.84±6.00	43.72±9.69	0.0001
Chol	177.51±27.24	218.63±37.73	0.0001
TG	88.69±30.04	119.0±40.38	0.001
HDL	44.20±12.28	34.26±6.9	0.0001
LDL	119.10±29.75	159.91±35.148	0.0001
HbA1c	5.14±0.69	7.83±1.70	0.0001
FBS	90.91±9.329	183.49+37.451	0.0001
LDL/HDL	2.88±0.975	4.96±1.842	0.001

Values are Mean ± SD. *P<0.05

Table 2.Correlation between inflammatory markers and lipid profile

	HDL	**LDL**	**TG**	**Chol**
TSA	r=-0.14	r=0.43	r=0.49	r=0.62
	P=0.431	P=**0.011**	P=**0.003**	P=**0.005**
Cp	r=-0.28	r=0.32	r=0.18	r=0.28
	P=0.11	P=0.06	P=0.30	P=0.10
CRP	r=0.12	r=0.15	r=0.13	r=0.19
	P=0.51	P=0.40	P=0.45	P=0.28

Table 3.Correlation between inflammatory markers and glycemic profile

Variable	**FBS**	**HbA1c**
TSA	r=0.046	r=0.20
	P=0.792	P=0.258
Cp	r=0.138	r=0.037
	P=0.429	P=0.83
CRP	r=0.198	r=0.08
	P=0.255	P=0.65

DISCUSSION

It was reported that low-grade inflammation exists in Diabetes mellitus and it is positively related with dyslipidemia (except for HDL cholesterol) in diabetics [13]. There is augmented inflammation in T2DM in Pakistani patients which plays role in higher insulin resistance in these patients. TNF-α levels increases with longer duration of the disease. Levels of inflammatory markers are not correlated to BMI, dyslipidemia or increasing age [21]. Raised serum IL-6 and TNF-α level in type 2 diabetic patients were found to be associated with increased BMI, fasting insulin levels and insulin resistance [22]. In a prospective study in American females, the baseline CRP and IL-6 levels were significantly higher in those who later developed T2DM [23] In the present study we have observed significant increase in Inflammatory markers CRP, Cp and TSA, Total cholesterol, TG, LDL cholesterol and HDL cholesterol was significantly decreased. Strong positive correlation was present between TSA and LDL (P=0.011), TSA and TG (P=0.003), TSA and Total cholesterol (P=0.005).A negative but insignificant correlation is found between TSA and HDL. No significant correlation was observed between inflammatory markers and glycemic profile.

LIMITATIONS AND FUTURE PERSPECTIVES

The major limitation of the present study was less sample size. Also, we have not studied male and female comparison. In our future studies, we plan a multi-centre study with study with higher sample size to confirm the results and also to observe male and female differences.

CONCLUSION

We conclude that, a strong association was present between inflammatory marker TSA and lipid profile. This study revealed that low grade inflammation is found in diabetic patients. The coexistence of metabolic syndrome and proatherogenic profile in T2DM needs urgent intervention as these can lead to future cardiovascular problems.

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