Status of Insulin Resistance and Interleukin-6 (IL-6) in Type- 2 Diabetic Subjects in Eastern Uttar Pradesh of India

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ABSTRACT

Introduction: Diabetes mellitus is a metabolic disorder characterized by hyperglycemia with disturbances of carbohydrate, fat and protein metabolism, resulting from defects in insulin action and secretion or both. The aim of the study is to evaluate the metabolic significance of type-2 diabetic subjects compared to healthy subjects and the independent factors associated with type-2 DM patients.

Material and methods: The study was conducted in M.L.N. Medical College, Allahabad (UP). A total of 258 cases were included in our study and diagnosis. Out of these, 158 were type-2 diabetic subjects and 100 were healthy individuals. They were evaluated by measurement of various blood parameters as FBS, HbA1c, TC, TG, HDL-c, LDL-c, VLDL-c, fasting Insulin, Insulin resistance by HOMA–IR calculation method, Tumour Necrosis Factor-α, Interleukin-6.

Results: An increase in the levels of FBS, HbA1c, TC, TG, HDL-c, LDL-c, VLDL-c, fasting Insulin, Insulin resistance by HOMA–IR, Tumour Necrosis Factor-α, Interleukin-6 level and a decrease in HDL was observed in diabetic groups. The value of all these study parameters were elevated in diabetes patients and the difference were found to be statically significant.

Conclusion: Raised levels of**,** Proinflammatory cytokines IL-6, TNF-α and fasting insulin are more frequently seen in type-2 diabetic patients. The Chronic hyperglycemia of diabetes is associated with the long-term consequences of diabetes that include damage, dysfunction and failure of various organs, which further lead to the development of cardiovascular problem, retinopathy, neuropathy, nephropathy etc.

Keywords: Type-2 DM (type-2 diabetes mellitus), IL-6 (Interleukin-6)

INTRODUCTION

The Chronic hyperglycemia of Diabetes is associated with the long term consequences of diabetes that include damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. 50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke). Diabetes causes about 5% of all deaths globally each year.[1] A close connection between insulin resistance and classic inflammatory signaling pathways has also recently been identified.[2] Insulin resistance is the driving force of hyperglycemia of type- 2 diabetes.[3] Several studies have demonstrated elevated levels of IL-6 individuals with insulin resistance.[4,5] The proinflammatory cytokines have also been shown to be elevated in type-2 diabetes. Proinflammatory cytokine IL-6 has been shown to have the strongest correlation with insulin resistance and type-2 diabetes.[6]

aims and objectives of the research were to know the level of inflammatory marker (IL-6) in type 2 diabetic subjects, to explore the status of biochemical parameters in type 2 diabetic subjects and to find out the correlation between biochemical and inflammatory marker in age and sex matched type 2 diabetic subjects.

MATERIAL AND METHODS

The study was carried out in the Department of Biochemistry M.L.N. Medical College, Allahabad between November 2013 and May 2015. All ethical measures were taken prior and during the study. The written consent of patients was also taken before starting the study. The study was done on 258 individuals, who included 158 type-2 diabetic subjects and 100 healthy individuals. All diabetic patients were on medication with oral hypoglycemic drugs. Age matched healthy control subjects were selected from known families. A record of clinical history and previous investigations of patients disorders were compiled in a proforma (Proforma enclosed). A proforma containing the relevant findings of clinical, biochemical and physiological investigations were recorded on preset questionnaire as base line record. The blood sample was analyzed for biochemical and immunological investigations which include: Fasting Blood Sugar (FBS), Glycosylated hemoglobin (HbA1c), Total Cholesterol (TC), Triglyceride (TG), High density-lipoprotein cholesterol (HDL-c), Low density lipoprotein cholesterol (LDL-c), Very low density lipoprotein cholesterol (VLDL-c), fasting Insulin, Insulin resistance by HOMA–IR calculation method, Interleukin-6. All parameters were given as mean± standard deviation (SD). The criterion for significance was $P < 0.05$. Pearson's correlation was used to evaluate the correlations between the variables. Data analyses were performed with the Statistical Package for the Social Sciences, version 16.0 (SPSS, Chicago, Illinois, USA).

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Study Variables	Control n=100	Uncontrolled type -2 diabetic n=158	t-value	P-Values
FBS(mg/dl)	76.42±12.32	166.09±37.7	5.42	<0.001
HbA_{1C} (%)	4.12±0.82	8.12±1.46	7.04	<0.001
Total Cholesterol (mg/dl)	162.72±21.09	253.94±44.62	9.08	<0.001
TG (mg/dl)	123.09±18.02	171.46±32.05	7.62	<0.001
HDL (mg/dl)	52.36±7.24	34.47±3.44	5.28	<0.01
LDL (mg/dl)	91.31±24.52	132.7±24.3	2.58	<0.01
VLDL (mg/dl)	25.58±4.19	54.89±16.8	1.96	<0.05
Fasting Insulin (µU/ml)	6.13±1.26	17.32±2.10	3.29	<0.001
HOMA-IR	1.34±0.30	5.47±1.24	2.57	<0.01
IL-6 (pg/ml)	8.85±1.46	18.32±4.86	5.68	<0.001

Table-1: Comparison of laboratory abnormalities between control healthy and uncontrolled type-2 diabetic subjects.

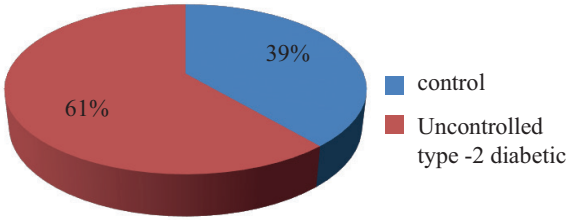

Figure-1: Showing the percentage of total number of subjects

RESULTS

The study included 100 healthy individuals and 158 controlled type-2 diabetic. The average age of the patients was 52 ± 8 years (Ranging from 36 to 74). Comparison of means of serum biochemical markers between healthy control and diabetic groups is presented in Table-1. The values of all these biochemical study parameters except HDL were elevated in uncontrolled diabetic patients as compared to healthy control group and the differences were found to be statistically significant (P value <0.05, <0.01 and <0.001). Values are given mean and standard deviation, mean difference is significant at P<0.05, mean difference is significant at P<0.01, mean difference is highly significant at P<0.001.

DISCUSSION

Chronic hyperglycemia in diabetes is associated with specific micro and macro-vascular pathology affecting many tissue and organs, causing retinopathy, nephropathy, neuropathy, cardiovascular diseases, and peripheral vascular diseases.[7,8] Our study showed FBS levels in uncontrolled diabetic groups (mean 166.09±37.7) were higher than healthy control group (mean 76.42±12.32), which confirmed the obvious dysglycemia in these patients (P value <0.001). Glycosylated hemoglobin was also increased in diabetic subjects.[9-11] The increase in HbA1c is due to high concentration of glucose present in both inside and outside the cells favouring the occurrence of spontaneous and non-enzymatic reactions between glucose and protein in intra and extracellular compartments resulting in advanced glycation end products.[12] We also observed that mean values of TC, TG, LDL-c and VLDL-c were found significantly increased whereas HDL-c was also found significantly decreased in uncontrolled diabetic groups as compared to control healthy group and the results were statistically significant. In a correlation coefficient analysis TC, TG, LDL-c and VLDL-c were also found to be positively correlated with uncontrolled diabetic population. This study is mainly focusing on the possible role of proinflammatory marker interleukin-6 along with insulin resistance in type -2 diabetic subjects. In our study we found that strong positive correlation of FBS with proinflammatory marker IL-6 in uncontrolled type 2 diabetic subjects. FBS was also positively correlated with HOMA-IR in uncontrolled diabetic subjects.

Both newly diagnosed or established patients with type-2 DM have shown that acute phase reactants and proinflammatory cytokines are positively correlated with insulin resistance.[13,14] Increase IL-6 levels have been linked to inhibition of hepatic glycogen synthase, activation of glycogen phosphorylase and lipolysis and increase triglyceride production.[15,16] As a result of these observations, it has been hypothesized that IL-6 plays a role as a glucoregulatory hormone.

CONCLUSION

In conclusion, the pathogenetic vision of diabetes mellitus has changed in the last few years, where inflammatory markers IL-6 and fasting insulin levels are playing pivotal roles in the development of Type-2 Diabetes Mellitus due to Insulin resistance and in the progression of complications in type-2 DM. These new pathogenic factors have lead to a considerable amount of new therapeutic approaches. Modulation of inflammatory processes in the setting of diabetes is now a days a matter of great interest.

FUTURE SCOPE

It is possible that in coming years the hope of new therapeutic strategies based on anti-inflammatory properties with beneficial actions on diabetic complications can be translated in to real clinical treatments.

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