Association of IL-6 with Diabetes Mellitus in Indian Population from Navi Mumbai

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Research Article

Abstract: Diabetes has already reached an epidemic level in India. Chronic inflammation has been considered as a culprit for setting pathophysiological changes which results in insulin resistance and type 2 diabetes mellitus. IL-6 is one of the several proinflammatory cytokines that have been associated with type 2 diabetes. Very few studies on role of circulatory IL-6 in diabetes have been published in Indians. This study aims to determine the serum levels of IL-6 in diabetic patients and compare them with healthy controls. We hypothesized that circulating IL-6 levels increases in diabetes due to underline chronic inflammation. **Conclusion:** Our results concluded that increased serum IL-6 levels compared to normal controls might be associated with inflammation related pathophysiology in type 2 diabetes.

Key words: Cytokines, IL-6, proinflammatory marker, Type 2 Diabetes.

Introduction

IL-6 is a multifunctional cytokine produced by the variety of cells including adipocytes, endothelial cells, smooth muscle cells, fibroblasts, lymphocytes and macrophages [1, 2]. Mechanism of action of IL-6 is under tight regulation while its high circulating levels has been associated with variety of diseases like obesity, diabetes and cardiovascular diseases [3]. It is a central mediator of acute phase response and stimulates production of hepatic CRP in liver [4]. In addition to this, IL-6 has been identified as a factor which is responsible for the development of insulin resistance. It has also been associated with the incidence of type 2 diabetes and other complications of diabetes like diabetic retinopathy [5] and as a marker of endothelial dysfunction [6], as it regulates the expression of adhesion molecules and other cytokines in endothelial cells. In a recent study Nguyen and colleagues identified IL-6 as an important biomarker for micro vascular complications in diabetes [7] and identified it as a mediator which can participate in the development of cardiovascular disease. Several studies were carried out on circulatory levels of IL-6 in type 2 diabetes but very few studies have been done on Indian patients. Most of these studies included Indian study participants which were residing in western countries where there life style, food habits, environmental factors were completely different than our Indian scenario.

Aim

The aim of the present work is to investigate the circulatory levels of IL-6 in type 2 diabetes and to correlate its circulatory levels with the traditional risk factors like lipid profile parameters and BMI with diabetes. The study has been carried out with Indian population residing in western part of India (Navi Mumbai).

Samples selection and Methods

The study involved 18 diabetic patients and 18 normal controls. Pregnant females, patients with chronic inflammatory diseases, cancer and rheumatoid arthritis were excluded from the study. Gender, age (years), height (cm), body weight (kg) were recorded for all the study subjects. Patients with newly diagnosed type 2 diabetes were included under diabetic group and age, sex matched controls subjects were included under normal group. Patients with other inflammatory diseases, cancer, rheumatic arthritis, sepsis, excessive obesity and pregnant women were excluded from this study. BMI was calculated as per the standard formula. BMI= Weight in Kg / Height in m^2. Fasting serum samples were collected from all the patients and controls included in the study and stored at -80^0 C. The biochemical parameters like fasting blood sugar, triglyceride (TAG) total cholesterol (TC), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were analyzed on an autoanalyser. The proinflammatory cytokine IL-6 was measured by ELISA kit according to the manufacturer's instructions.

Statistical Analysis

Statistical analysis was performed using SPSS 16.0 software. Results are expressed as means and ± SD. Independent t-test was used to compare the means of the variables between diabetic patients and control subjects.

Results

The clinical and biochemical characteristics of the Diabetic patients and normal controls are summarized in Table 1.There was no significant difference was noted between two groups, diabetic and controls with respect to age (53.94 ± 8.84 vs. 52.50 ± 9.52) as participants from both the age groups shows similar age. A significant difference was observed related to BMI (25.61± 1.41 vs. 22.16 ± 1.82). Blood sugar was significantly higher in diabetic patients compared to controls (181.72 ± 71.48 vs. 100.44 ± 10.70) which suggest derangements in glucose metabolism. Among lipid profile parameters, only HDL showed significant decrease in diabetic group than control (42.33± 5.46 vs. 49.50 ± 6.83). IL-6 circulating levels were highly elevated in diabetic group than our control subjects (6.24 ± 2.35 vs. 2.6 ±0.51). This shows the high inflammatory status of the body. While Serum TAG, Cholesterol and LDL levels were significantly different in both the groups (167.89± 38.87 vs.142.94 ±20.23 mg/dl), (175.56±20.48 vs. 160.56 ± 20.20 mg/dl) and (99.22 ± 19.40 vs. 82.61 ±22.49 mg/dl) respectively, when compared between diabetic and normal controls.

Table1: Independent t-test applied for all study parameters in diabetic and control groups

	Diabetic (18)	**Control(18)**	**P Value**
Age	53.94(±8.84)	52.50(±9.52)	0.640*
Sex	09(M) 09(F)	09(M) 09(F)	----
BMI	25.61(±1.41)	22.16(±1.82)	0.000**
FBS mg%	181.72(±71.48)	100.44(±10.70)	0.000**
TAG mg%	167.89(±38.87)	142.94(±20.23)	0.021**
TC mg%	175.56(±20.48)	160.56(±20.20)	0.034**
LDL mg%	99.22(±19.40)	82.61(±22.49)	0.024**
HDL mg%	42.33(±5.46)	49.50(±6.83)	0.001**
Sr. IL-6 (pg/ml)	6.24(±2.35)	2.6(±0.51)	0.000**

*NS- Non Significant >0.05** S- Significant < 0.05

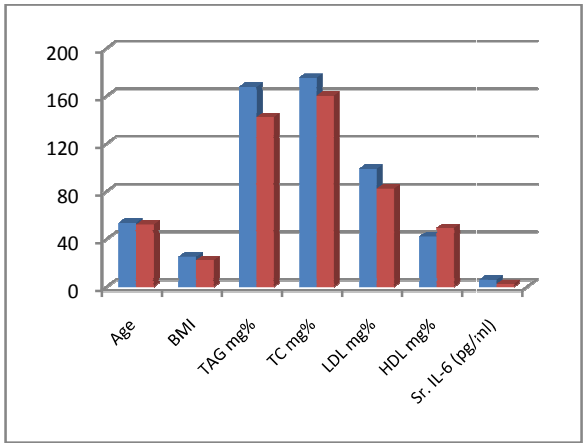

Figure 1: Comparison of various study parameters in diabetic and control group

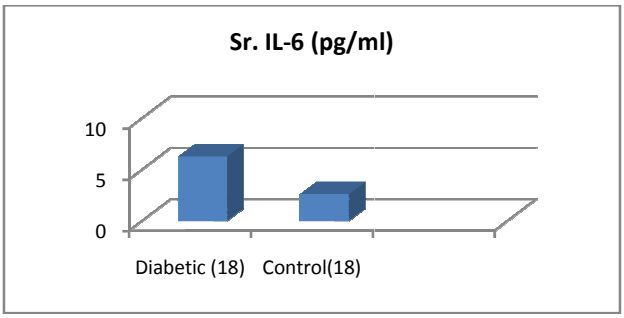

Figure 2: Comparative graphical representation of serum IL-6 levels in diabetic and control group

Discussion

The main finding of this study reveals significantly higher levels of IL-6 in diabetic group than the control subjects. Similar to previously reported studies [8, 9, 10], the results have shown an increased inflammatory status in type 2 diabetes. Among lipid parameters HDL showed highly significant low levels in diabetic subjects compared to controls. While other lipid parameters showed moderate significant difference between these two groups. This reveals the role of scavenging HDL in reverse cholesterol transport, its depletion in diabetic patients indicates its role in disturbance in cholesterol transport.

Previous studies have shown that circulating levels of IL-6 were high in type 2 diabetic patients [8, 9]. Similar findings were reported in the present study. In vivo and vitro effect of IL-6 were studied by Bastard *et al* in 2002 on glucose uptake and insulin resistance. They concluded that IL-6 might be one of the factors which have been involved in development of insulin resistance [10]. Further in 2003, Rotter *et al*, have shown a similar relationship between IL-6 and insulin resistance [11]. It has been noted that IL-6 impairs the insulin signaling pathway in hepatocytes. It is stated that increased levels of serum IL-6 during inflammation activates JAK-2/STAT-3 inflammatory response and play an important role in insulin resistance [12]. In adipocytes it mediates its effects via stimulation SOCS-3 expressions [13] while in skeletal muscle role of IL-6 has not been understood yet. According to a study time and dose dependent exposure of skeletal muscle to IL-6 may alter the insulin sensitivity of skeletal muscle [14]. A study carried out in 2005 reported that depletion IL-6 improves hepatic insulin resistance. Determination of serum IL-6 can be used for the identification of diabetic patients with high risk of future cardiac events as it stimulates production of CRP [15]. Ridker *et al* studied the inflammatory signaling and suggested IL-6 as the marker of endothelial damage in elderly men [16]. According to some research groups, IL-6 is just an inflammatory marker which can determine the systemic inflammatory status. However taking in the

account the pleiotropicity of this cytokine and its wide array of actions on various cell types, the high inflammatory signaling mechanisms may precipitate the existing systemic and local inflammatory mechanism.

Conclusion

The study results showed higher concentrations of serum IL-6 in diabetic group when compared with control. It suggests that lL-6 being an inflammatory mediator might be responsible for some underline changes which may contribute for the development of type 2 diabetes. Further studies on role of IL-6 as an inflammatory mediator in a homogeneous population of diabetic patients may focus some more light on its role in the development of Type 2 diabetes.

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Disclosure

No conflicts of interest are declared by the authors.

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