IL-6: AN IMPORTANT MEDIATOR OF OBESITY BASED INFLAMMATION

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Abstract— **Obesity is a global health problem. Excessive fat mass is considered as culprit for stimulating inflammatory mechanisms. Recently adipose tissue came into lime light when it was recognized as a biggest endocrine organ which secrets variety of bioactive substances known as adipokines and cytokines. Hence obesity is now also recognized as an inflammatory condition where adipose tissue secretes various inflammatory markers. Interleukin-6 (IL-6) is among them. It has been also known that IL-6 is an important pro-inflammatory cytokines in the pathogenesis of Insulin resistance (IR), type 2 diabetes and atherosclerosis. In this study the inflammatory status of obese subjects was determined by exploring the differences in serum levels of inflammatory marker IL-6, between control subjects and obese individuals. Our result showed higher levels of serum IL-6 in obese compared with non obese individuals. From this study it is concluded that IL-6 levels increased significantly in obese subjects than normal healthy controls.**

Keywords— **Obesity, pro inflammatory cytokine, IL-6, BMI and Lipid profile**

I. INTRODUCTION

In India obesity guidelines have been revised due to occurrence of CAD in at a lower BMI as compared to the international standards. Hence in 2008 Health Ministry, Diabetes foundation of India, Indian medical council, All India institute of Medical Science, National Institute of Nutrition and 20 other organizations jointly revised the obesity scale (1). Now BMI 23 is considered as overweight compared to earlier level 25, BMI 25 will be considered clinically obese compared to earlier level of 30. Obese patients have excess fat depots; to store this excessive fat mass adipocytes expansion leads to hypertrophic adipocytes (2). This results in hypoxia which is one of the factors responsible for angiogenesis and stimulates expression of various angiogenic factors (3). Hypoxia has been also associated with increased production of inflammatory cytokines including IL-6 (4) which in turn stimulates various cell adhesion factors. For the present study it was hypothesized that serum IL-6 levels increases in obesity.

IL-6 is a pro inflammatory cytokine mainly secreted by adipose tissue. It is encoded by IL-6 gene. IL-6 is a pleiotropic cytokine and considered to be involved in various pro inflammatory signalling mechanisms (5). IL-6 signals through a cell-surface type I cytokine receptor complex consisting of the ligand-binding IL-6Rα chain (CD126), and the signal-transducing component gp130 (6). IL-6 mediates its effects via various mediators which are common for various other cytokine signalling that make IL-6 signalling a complex affair. IL-6 may alter the insulin sensitivity and has been associated with development of insulin resistance and type 2 diabetes (7,8). Some studies reported its association with cardiovascular diseases (9). It has been studied that increased IL-6 concentration sets a toxic environment for arteries (10). Farb and colleagues concluded that overall adiposity showed a significant relation with cell adhesion molecules than IR. IL- 6 has been involved in modulation of cell adhesion molecule expression (11).

Very few studies were reported in India which included evaluation of IL-6 in obesity while not a single study is reported from Navi Mumbai area. Changing lifestyle, dietary habits and sedentary workload enhances excess accumulation of fat which begins inflammatory cascade. Hence people may suffer from obesity based other pathological conditions like IR, type 2 diabetes as well as CAD even in their 30s. Detail understanding of these inflammatory markers and their signalling mechanism may provide a clear picture of the sub cellular events which further propagates these inflammatory signalling.

II. AIM

Aim of the present study is to evaluate the circulatory levels of IL-6, lipid profile, BMI and to compare them between obese and control groups.

A. Samples selection and Methods

Fasting blood samples were collected from all the subjects included in the study groups- Obese and control. Only obese participants were included in obese group while, obese

diabetic and obese hypertensive subjects were excluded from this study. Anthropometric examination was conducted in a fasting state and BMI was calculated according to the standard formula, BMI=Weight in kilograms/ Height in meters. Serum was frozen in aliquots at -80°C immediately after centrifugation. Lipid profile parameters were measured by commercially available kits using Automated- Clinical Chemistry Photometric analyser. Finally serum levels of IL-6 were measured using ELISA kit.

Information consent was collected from all the included study subjects and the study was approved by the university ethical committee of Pad. Dr. D.Y. Patil University, Navi Mumbai.

B. Statistical Analysis

Statistical analysis was performed using SPSS 16.0 software. Results are expressed as means ± SD. Independent t-test was performed to compare the means of the variables.

III. Results

The clinical and biochemical characteristics of the obese patients and normal controls are summarized in Table 1.

TABLE I
DESCRIPTIVE STATISTICS OF ALL STUDY PARAMETERS IN DIABETIC AND CONTROL GROUPS.

	Obese(18)	**Control(18)**	**'p' Value**
Age	52.44(±10.7)	52.50(±9.61)	0.04
Sex	09(M)/ 09(F)	09(M)/ 09(F)	---
BMI	27.56(±1.4)	22.51(±1.87)	0.00
TAG mg%	177.78(±35.34)	142.44(±20.16)	0.01
TC mg%	172.28(±22.05)	160.5(±20.21)	0.00
LDL mg%	93.0(±20.12)	82.51(±22.45)	0.00
HDL mg%	43.39(±4.74)	49.50(±6.83)	0.00
Sr. IL-6 (pg/ml)	5.38(±2.5)	2.6(±0.51)	0.00

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

The two groups (obese and control) significantly differ with respect to mainly BMI and all other lipid profile parameters. IL-6 circulating levels were highly elevated in obese group than control subjects (5.38 ± 2.5 vs. 2.6 ±0.51 pg/ml). However serum TAG (177.78 ± 35.34 vs. 142.44 ± 20.16 mg/dl), Cholesterol (172.28 ± 22.05 vs. 160.5 ± 20.21 mg/dl), LDL (93.0 ± 20.12 vs. 82.51 ±22.45 mg/dl) and HDL levels (43.39 ± 4.74 vs. 49.50 ± 6.83 mg/dl) were significantly differ in obese and control groups respectively.

The above mentioned results suggested that in obese group derangements in lipid profile parameters and increased circulatory IL-6 levels indicate an increased inflammatory status. Chronic inflammation may stimulate various inflammatory signalling pathways via increased production of inflammatory mediators like IL-6.

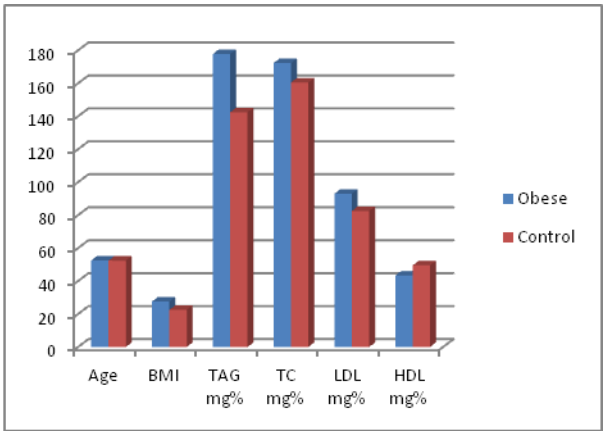

Fig.1 Bar diagram of various study parameters in diabetic and control group

In Fig. 1 compares all the study parameters between the obese and the control groups. Obese group showed statistically significantly values for BMI and other parameters of lipid profile. Serum IL-6levels were also showed highly significant difference between the two groups.

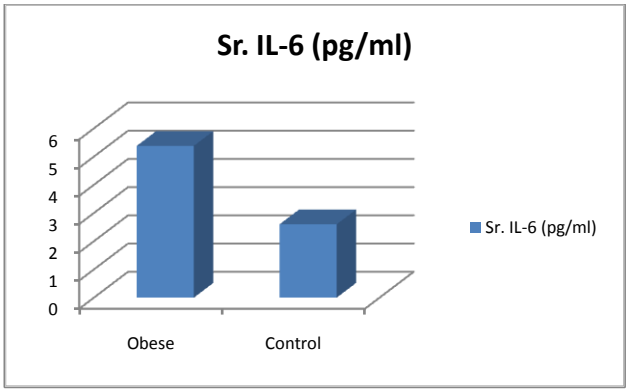

Fig. 2 Comparative graphical representation of serum IL-6 levels in obese and control groups.

Fig. 2 compares circulatory levels of IL-6 in obese participants and control subjects. It shows a higher level of serum IL-6 in obese patients than normal controls and suggests role of IL-6 in obesity related inflammation.

IV. Discussion

The study results suggested that increased circulatory levels of IL-6 were associated with obesity based inflammation. It has been considered that IL-6 may be involved in promoting inflammation among obese subjects. Similar observations were noted by previous studies which supports our study results (6). Present study observed a significant difference between the BMI of obese participants and control subjects. BMI is has been used commonly to categorise obesity. Adipose tissue expansion to store excessive fat has been considered as a crucial event which ultimately secrets high amounts of IL-6 via hypoxia mediated stimulation of IL-6 synthesis (12). It was reported by previous studies that hypoxia stimulates various pro inflammatory adipokine-cytokine secretions and IL-6 is among them (13). According to Halberg et al, hypoxia initiates adipose tissue dysfunction and also responsible for lowering insulin sensitivity of adipose tissue (14). Higher circulatory IL-6 levels were observed in obese participants than control subjects suggested the inflammatory environment of obese participants. A chronic inflammatory environment in obesity due to increased IL-6 levels, a proinflammatory stage has been set which can leads to various pathophysiological changes and might results in insulin resistance, type 2 diabetes (7,8) and even cardiovascular diseases (9,15). All these studies suggested a possible link between the obesity and other related pathological conditions. The higher inflammatory environment in the obese participants associated with higher IL-6 levels than normal could play a crucial role in propagating inflammatory signalling.

V. Conclusion

In conclusion the present study reported that circulatory IL-6 levels were found to be increased in obesity. Preventive action should begin urgently and lifestyle changes such as weight control and exercise are among first steps to be taken. Further work is now awaited to confirm these findings in larger series, as well as to investigate the potential role of IL-6 in early therapeutic intervention in the obesity.

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Disclosure

The authors report no conflicts of interest.

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