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Original Article

Interleukin-10 as a novel biomarker of metabolic risk factors

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ABSTRACT

Background: Interleukin-10 (IL-10) is an adipocytokine that is abundantly expressed in visceral fat tissue. We investigated the association of interleukin-10 with the number of metabolic risk factors.
Finding: The study population comprised 220 children who underwent annual health checkups. Plasma Interleukin-10 levels were determined by enzyme-linked immunosorbent assay. We divided the subjects into 4 groups according to Interleukin-10 levels. A reduction of plasma interleukin-10 levels significantly correlated with an increase in the mean number of metabolic risk factors such as increased waist circumference, BMI, dyslipidaemia, high blood pressure and glucose intolerance.
Conclusions: Circulating Interleukin-10 levels negatively correlated with the multiplicity of metabolic risk factors, suggesting that IL-10 acts as a biomarker of metabolic disorders.

1. Introduction

The prevalence of obesity in both children and adults has increased over several decades in developing and developed countries. In terms of estimates, 200 million school-age children are overweight and 40–50 million of them are obese. According to literature available, 70% of obese adolescents become obese in adult life [1]. The prevalence of overweight was estimated 12.64% and that of obesity to was 3.39% in 2012 in meta-analysis of Indian children [2]. The overall prevalence of overweight and obesity was 18.2% by the International Obesity Task Force (IOTF) classification and 23.9% by the WHO standards in India [3].

Childhood obesity, affected morbidity and mortality significantly if sustained through adulthood [4]. In recent years, increasing in frequency of childhood obesity and type 2 diabetes mellitus (DM) parallelly increase the prevalence of metabolic syndrome (MS) [5,6]. The prevalence of MS in childhood was reported approximately 10%, while this rate climbs to 30–50% in overweight or obese children (39% in moderately and 49% in severely obese adolescents) [6].

In addition to genetic and environmental factors, the modification of nutritional patterns, decreased physical activity and the adoption of sedentary lifestyles have been affected the underlying risk factors for obesity [7]. Increase in the severity of obesity predisposes to the development of complications, including components of MS [8].

Obesity, deposition of fat at visceral adipose tissue, is causally linked with a cluster of metabolic disorders including glucose intolerance, dyslipidaemia, and hypertension commonly called metabolic syndrome [9]. Adipose tissues are an active endocrine organ that produce various adipocytokine. In obese individuals many adipokines are produced in excess which potentially promotes metabolic function [10]. Fat tissues also produce a smaller number of adipocytokines such as IL-10, which may play an important role for development of obesity [10,11]. The imbalance production of adipocytokines may also cause the development of obesity related metabolic disorders.

Proinflammatory cytokines, such as tumor necrosis factor (TNF-α) and interleukin (IL)-6, might impair insulin action [12]. Although their level has been shown to be increased in obesity [13] but nothing is known about the role of potent anti-inflammatory cytokines IL-10 (major inhibitor of cytokine synthesis) in development of metabolic disorders. It suppresses macrophage function and inhibits the production of proinflammatory cytokines [14]. Recent studies in animals have shown a protective role of IL-10 in atherosclerotic lesion formation [15]. Recent studies provided evidence that IL-10 might exert some beneficial metabolic effects [16,17].

Until now there have been no reported studies that evaluated circulating IL-10 levels in childhood obesity, nor have potential

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associations between serum IL-10 concentrations and the obesity been tested in children till date. The aim of the present study was to examine the relationship between circulating plasma IL-10 concentration and it's association with the development of metabolic disorders in children.

2. Material and methods

2.1. Subject's selection and study design

We studied 220 obese children (82 males and 138 females) of age group 5–11 years and 12–17 years. They were recruited from those attending the camp for obesity and weight management at the Department of Physiology, King George Medical University, Lucknow between oct 2013 to sep 2017. From them few were selected by conducting obesity awareness camps in schools of Lucknow District. The age and gender adjusted body mass index (BMI) ≥ 85th percentile (according to National Cholesterol Education Program (NCEP-ATP III) were enrolled in the study [18]. Children were free from psychiatric problems and none took any drug. They were recruited excluding any secondary to endocrinological, genetic disorder, having any viral or bacterial infection, any respiratory or inflammatory diseases or other systemic diseases and pharmacological agents, as well as those on medication. Each child and their family gave informed consent to participate in the study, which was approved by the institutional committee of ethical practice of our institution.

2.2. Definitions

Metabolic syndrome (MetS) was diagnosed by the modified National Cholesterol Education Program-Adult Treatment Panel-III (NCEP-ATPIII) criteria [18].

2.3. Clinical and biological measurements

Children with three or more of the following criteria were defined as having the metabolic syndrome**: (1) Abdominal obesity:** (a) Overweight: BMI 85–94th percentile, (b) obese BMI: 95–98th percentile, (c)severally obese BMI: >98th percentile (2–20 years, Centres for Disease Control and Prevention [CDC] growth charts, United States) [19].

2) Hypertrigly ceridemia: High TG (≥90th percentile for age and sex) or ≥150 mm of Hg.

3) Low high-density lipoprotein (HDL) cholesterol: Low HDL-C levels (<5th percentile for age and sex) or <40 mg/dl in male children and <50 mg/dl in female children.

4) High blood pressure: systolic/diastolic blood pressure ≥90th percentile for age and sex or elevated systolic BP ≥ 130 mm of Hg and diastolic BP ≥ 85 mm of Hg.

5) High fasting glucose: FG ≥ 100 mg/dl.

All children were studied after a 14-h overnight fast. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. The degree of obesity was determined using BMI percentile or z-scores. The BMI percentile and z-score were calculated by online BMI-for-age CDC software with the Lambda, Mu, Sigma (LMS) method [20] and the subjects were divided into four groups according to their BMI percentile **(a) 5–84 percentile or z-score 1.65–1.99:** Healthy weight or without metabolic syndrome, **(b) 85–94 percentile or z-score 2–2.49:** overweight, **(c) 95–98 percentile or z-score 2.50–2.99:** obese and **(d) >98 percentile or z-score ≥3:** severally obese, respectively. Besides the BMI children were also examined for blood pressure, waist circumference (cm).

Routine biochemical analyses such as fasting blood glucose, lipid profile of all subjects was assessed in the hospital's biochemistry laboratory. Fasting plasma Insulin was estimated by Immuno-radiometric assay method (Immunotech Radiova, Prague). Serum samples for IL-10 were stored at −80 °C and were assayed in duplicate using a high sensitivity, quantitative sandwich enzyme assay by using Human IL-10 ELISA Kit (Interleukin-10, ab46034 abcam, Canada). The lower limit of detection was 12.5 pg/ml.

2.4. Statistical analysis

Continuous variables and IL-10 value are expressed as means ± standard deviation (SD); and categorical variables as frequencies and percentages. Using the healthy group as control, the differences in baseline characteristics were tested using the Student's test for continuous data and Chi-square test for categorical data at 95% confidence interval. ANOVA were used to analyzed the significance equality of mean, relationship between the number of metabolic risk factors and interleukin-10 levels and contribution of changes in the BMI with IL-10. A value of $p < 0.05$ was considered significant. All calculations were made on an IBM PC computer (SPSS, version 20.0, SPSS, Inc., Chicago, IL).

Table 1
Clinical characteristics of the two subgroups with and without metabolic syndrome.

Characteristics	Without MS(n = 100) (45.45%)	With MS (n = 120) (54.54%)	P Value
Weight (Kg)	37.96 ± 9.54	44.98± 12.45	<0.001
Height (cm)	144.19 ± 13.87	133.54 ± 16.21	<0.001
BMI (Percentile)	54.75 ± 12.67	94.66 ± 4.08	<0.001
BMI z-score	0.14 ± 0.35	1.80 ± 0.58	<0.001
Age (Years)	11.23 ± 2.77	10.72 ± 2.97	0.189
Systolic BP (mm Hg)	105.83 ± 9.53	114.88 ± 7.29	<0.001
Diastolic BP (mm Hg)	68.32 ± 7.14	77.16 ± 5.66	<0.001
Waist circumference(cm)	74.26 ± 7.81	78.59 ± 8.10	<0.001
Fasting glucose, mg/dl	107.42 ± 4.45	115.02 ± 12.51	<0.001
Blood Glucose(PP)	151.03 ± 15.40	145.96 ± 3.13	0.001
Triglycerides (mg/dl)	103.09 ± 13.86	114.63 ± 9.86	<0.001
Total cholesterol (mg/dl)	184.80 ± 7.71	188.51 ± 24.88	0.153
LDL-cholesterol (mg/dl)	121.19 ± 7.99	122.83 ± 24.23	0.517
HDL-cholesterol (mg/dl)	42.59 ± 4.09	42.66 ± 6.12	0.919
VLDL-cholesterol (mg/dl)	20.6182 ± 2.77	23.0975 ± 0.72	<0.001
IL-10 Conc. (pg/ml)	17.78 ± 5.51	7.53 ± 1.32	<0.001

MS = metabolic syndrome; BMI = body mass index, LDL = low-density lipoprotein; HDL = high-density lipoprotein; VLDL = very-low-density lipoprotein. Values are mean ±SD