Diabetes & Metabolic Syndrome: Clinical Research & Reviews 8 (2014) 152–155

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Imbalance between protective (adiponectin) and prothrombotic (Plasminogen Activator Inhibitor-1) adipokines in metabolic syndrome

Ashok Kumar Ahirwar [a,*], Anju Jain [a], Binita Goswami [a], M.K. Bhatnagar [b], Jayashree Bhatacharjee [c]

[a] Department of Biochemistry, LHMC, New Delhi, India
[b] Department of Medicine, LHMC, New Delhi, India
[c] VMMC, New Delhi, India

ARTICLE INFO

Keywords:
Metabolic syndrome
Adiponectin
Plasminogen Activator Inhibitor-1

ABSTRACT

Aims: The metabolic syndrome (MS) consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus (DM). Visceral adipose tissue actively produces a variety of adipokines that interact in various obesity related disorders such as metabolic syndrome, diabetes mellitus and heart diseases. Adiponectin has protective role in the vascular physiology while Plasminogen Activator Inhibitor-1 (PAI-1) has a prothrombotic and consequent deleterious effect on the endothelium. We attempted to assess the putative imbalance if any between these two mediators in subjects with metabolic syndrome in the Indian context.

Materials and methods: We enrolled 50 diagnosed case of metabolic syndrome as per International Diabetes Federation (IDF) criteria and 50 healthy volunteers as control. Clinical evaluation included anthropometric, routine biochemical analysis as well as adiponectin and PAI-1 measurement.

Result: Subject with MS had significantly lower adiponectin (9.8 ± 1.0 vs 16 ± 1.1 μg/ml) and higher PAI-1 (232 ± 87 vs 185 ± 96 ng/ml). A statistically significant correlation was observed between adiponectin and HDL levels ($r = 0.388$, $p = 0.005$).

Conclusion: Subjects with MS have lower adiponectin and higher PAI-1 levels as compared to controls. The subsequent tilt toward a more prothrombotic and pro inflammatory milieu in the vascular endothelium may be pathognomonic of metabolic syndrome. This understanding of the still undiscovered subtle vascular alterations may help in the better management of obesity and MS.

1. Introduction

The metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus (DM). The major features of metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia, and hypertension [1].

Prevalence of metabolic syndrome varies across the globe and numerous studies have been conducted to estimate the same in different ethnic groups. Its prevalence varies from 8 to 24.2% [2,3] in males and from 7 to 46.5% [4,5] in females. It is estimated that around 20–25% of the South Asian population has metabolic syndrome [6]. In India its prevalence varies from 24.9% in Northern India to 41% in Southern India [7].

The metabolic syndrome represents combined occurrence of atherogenic dyslipidemia, insulin resistance, elevated blood pressure and central adiposity. Pro-inflammatory and prothrombotic state contributing to endothelial dysfunction is a common feature in metabolic syndrome [8]. The etiology of metabolic syndrome is complex, determined by the interplay of both genetic and environmental factors. Insulin resistance and visceral obesity have been recognized as the most important pathogenic factors [9].

Visceral obesity is a key component in the development of the metabolic syndrome. Increased central adiposity, particularly in visceral region, leads to greater free fatty acid flux and inhibition of

* Corresponding author at: Department of Biochemistry, House Surgeon Block, Lady Hardinge Medical College, Room No. 331, Shaheed Bhagat Singh Marg, New Delhi 110001, India. Tel.: +91 09654210832.
E-mail address: drashoklhmc@gmail.com (A.K. Ahirwar).

http://dx.doi.org/10.1016/j.dsx.2014.04.035
1871-4021/

insulin action. Adipose tissue in obesity is resistant to insulin action which is associated with disturbed glucose metabolism in the muscles and liver.

Visceral adipose tissue actively produces a variety of locally and systemically functioning bioactive molecules (adipokines) [10–12], that have diverse actions on metabolism, insulin sensitivity, immunity, angiogenesis, blood pressure and hemostasis [8].

Adiponectin has anti-inflammatory property which has been considered as a key regulator of insulin sensitivity and tissue inflammation. This protein synthesized exclusively by adipocytes and present at very high concentrations in the blood but its level inversely correlates with the amount of body fat. Adiponectin may act as a signaling molecule to regulate insulin action in the liver (improve hepatic insulin sensitivity) and skeletal muscle (increase fuel oxidation) [8]. In type 2 diabetics adiponectin is significantly reduced. Protective role of adiponectin within the arteries results from suppression of the inflammatory processes such as adhesion, proliferation, phagocytosis and deposition of lipids in monocytes [8].

Plasminogen Activator Inhibitor-1 (PAI-1) is a prothrombotic adipokines which is an important inhibitor of the fibrinolytic system, so elevated levels could suppress fibrinolysis and result in an increased risk of thrombosis [13,14].

Most of adipokines such as PAI-1 are upregulated in metabolic syndrome. In contrast, there are a smaller number of adipokines such as adiponectin which exerts beneficial actions on obese complications with anti-inflammatory properties. Thus, metabolic syndrome is result of the imbalance in the production of pro-inflammatory and anti-inflammatory adipokines under conditions of obesity.

2. Materials and methods

Our study was conducted in the Department of Biochemistry in collaboration with the Department of Medicine, Lady Hardinge Medical College & Smt. Sucheta Kriplani Hospital, New Delhi after approval by the Ethical Committee of LHMC, New Delhi.

We enrolled 50 cases of metabolic syndrome (diagnosed as per IDF Guidelines) and 50 age and sex matched healthy controls. The IDF Guidelines as follow: central obesity (waist circumference: ≥90 cm for males and ≥80 cm for females). Plus any two or more of the following: hypertriglyceridemia-fasting triglycerides ≥150 mg/dl or specific medication, low HDL cholesterol: ≤40 mg/dl (males), and ≤50 mg/dl (females), or specific medication, hypertension: blood pressure ≥130 mmHg systolic or ≥85 mmHg diastolic or previous diagnosis or specific medication and fasting plasma glucose ≥100 mg/dl or specific medication or previously diagnosed type 2 diabetes. If BMI is >30 kg/m^2, central obesity can be assumed and waist circumference does not need to be measured. Subjects with hepatic disease, renal disease, other endocrine diseases, alcoholism, infectious diseases or receiving any medication were excluded.

Bilingual informed written consent was taken from the patients. Detailed clinical history with special reference to metabolic syndrome and thorough clinical examination of patient was conducted. Necessary anthropometric measurements were taken which include height, weight, waist circumference, hip circumference, body mass index and waist hip ratio.

Five milliliter of venous blood sample was collected from the subjects under sterile conditions after overnight fasting. The blood samples were processed immediately for separation of plasma and serum. For adiponectin, Plasminogen Activator Inhibitor-1 and insulin measurements, serum were stored in aliquot at −40 °C. For routine hematological and biochemical investigations, samples were immediately analyzed by using Automated clinical chemistry analyzer (Beckman Coulter systems; CX series) by standard Kits and reagents. Electrolytes were measured by ISE method using Roche AVL 1980. Adiponectin in plasma was determined by sandwich ELISA method using the commercially available, human Adiponectin Enzyme Immuno Assay kit by DRG International Inc. (USA). PAI-1 in plasma was determined by sandwich ELISA method using the commercially available BioVendor ELISA kit (Czech Republic). Insulin level by chemiluminiscent based immunoassay (CLIA) on Beckman Coulter Access 2 Immuno-assay system by using closed system Beckman reagent kit. Repeated freeze–thaw cycles were avoided. HOMA-IR model was used to calculate the insulin resistance by formula: HOMA-IR = serum glucose (mg/dl) × plasma insulin (μU/ml)/405.

Table 1
Demographic and anthroprometric parameters of study population.

Parameters	Cases (n = 50) (mean ± SD)	Control (n = 50) (mean ± SD)	p value
Height (m)	1.56 ± 0.08	1.64 ± 0.11	0.000*
Weight (kg)	68.9 ± 13.5	68.1 ± 13.3	0.755
BMI (kg/m^2)	28 ± 5.4	25 ± 4.4	0.002*
Waist circumference (cm)	99 ± 8.9	92 ± 8.9	0.001*
Hip circumference (cm)	103.8 ± 12.4	99 ± 8.5	0.041*
Waist hip ratio	0.96 ± 0.09	0.93 ± 0.04	0.025*
Systolic BP (mmHg)	132 ± 12	122 ± 9	0.000*
Diastolic BP (mmHg)	86 ± 8	81 ± 5	0.001*

* p value≤0.05 is considered statistically significant.

3. Statistical analysis

All statistical analyses were performed with the SPSS software programme version 20. For comparison of variables with a normal distribution unpaired, 2-tailed Student's t-test and Pearson's correlation were used. A $p \leq 0.05$ was considered statistically significant. Logistic regression analysis was used to identify association with metabolic syndrome.

4. Results

The anthropometric and basal clinical findings are compared in Table 1. The mean BMI along with waist hip ratio were significantly higher in the cases as compared to the controls. The mean blood pressure of the cases in the study group was significantly higher than the mean blood pressure of the subjects in the control group (132/86 ± 12/8 mmHg vs 122/81 ± 9/5 mmHg). Table 2 highlights the biochemical profile of the study population. The mean serum triglyceride levels in the study group (182.7 ± 112 mg/dl) were significantly higher than the control group (141.5 ± 64.8 mg/dl). The difference in HDL levels between the study (38.8 ± 10 mg/dl) and

Table 2
Biochemical profile of study population.

Parameters	Cases (n = 50) (mean ± SD)	Controls (n = 50) (mean ± SD)	p value
Total cholesterol (mg/dl)	240.7 ± 91.5	246.5 ± 87	0.781
Triglyceride (mg/dl)	182.7 ± 112	141.5 ± 64.8	0.026*
HDL (mg/dl)	38.8 ± 10	49.2 ± 11	0.00*
LDL (mg/dl)	36.5 ± 22.4	28.3 ± 13	0.026*
VLDL	38.6 ± 10	49.1 ± 11.2	0.023*
TC/HDL	6.6 ± 2.89	5.3 ± 2.33	0.015*
TG/HDL	5.02 ± 3.59	3.06 ± 1.75	0.001*
LDL/HDL	4.52 ± 2.51	3.66 ± 2.16	0.070*
FPG (mg/dl)	181.3 ± 70.9	96.3 ± 7.5	0.000*
PPBG (mg/dl)	232.4 ± 94	140.74 ± 142	0.000*
HbA1c (%)	8.56 ± 2.73	5.56 ± 0.99	0.000*
Insulin (μIU/ml)	14.6 ± 13	6.6 ± 3	0.000*
HOMA-IR	6.4 ± 7.1	1.62 ± 0.753	0.000*

* p value ≤ 0.05 is considered statistically significant.