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Original Article

Association of acylation stimulating protein and adiponectin with metabolic risk marker in North Indian obese women

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ABSTRACT

Background: Plasma concentrations of Acylation stimulating protein (ASP) and adiponectin are associated with body weight and energy homeostasis. The purpose of this study is to describe the potential role of acylation stimulating protein and adiponectin with metabolic risk marker in North Indian obese women.

Methods: This is a case control study. Total 520 women were recruited for the study n = 260 women with obesity (BMI>30) study group and n = 260 women without obesity (BMI<25) control group. Serum ASP and adiponectin level were determined by enzyme linked immunosorbent assay.

Results: Result indicated that WC, BP, lipid profile, FPG, FPI, IR (HOMA-IR), ASP were significantly higher but adiponectin and HDL were significantly lower in women with obesity than in women without obesity. Furthermore ASP was significantly positive correlated with WC, FPG, TG, VLDL, FPI and IR, whereas the correlation of adiponectin was significantly negative correlated with WC, FPG, TG, IR, ASP and significantly positive correlated with HDL in women with obesity.

Conclusion: The study shows that high level of ASP and low level of Adiponectin could be a potential marker of women with obesity among metabolic syndrome.

1. Introduction

Obesity is one of the key risk factors of metabolic disorders: type 2 diabetes, metabolic syndrome and coronary heart disease [1], obesity is a multi factorial state of excessive fat involving environmental, genetic, physiologic, metabolic, behavioural, and psychological components [2]. Metabolic syndrome refers to the clustering of a number of risk factors (obesity, hypertension, dyslipidaemia and hyperglycaemia) believed to be related to insulin resistance [3,4]. Increase in incidence of overweight and obesity are associated with metabolic disorders are a global public health concern which affects 45% of Indian population [5]. Women are often more likely to be overweight in general because of hormonal factor are responsible in weight gain and central obesity that increase fat mass of abdomen which is associated with dyslipidemia, insulin resistance, hypertension [6]. Adipose tissue secretes various adipocytokines and hormones alteration of these hormone, play a important role in the metabolic disorder [7] (see Tables 1–4).

ASP is adipocyte derived hormone that reflects the amount of body fat in the human being, involved in energy homeostasis and insulin resistance [8]. Adiponectin is another harmone secreted from adipose tissue which is downregulated in obesity [9], their low level cause of insulin resistance and type-2 diabetes. Acylation stimulating protein (ASP) is an adipose tissue originate lipogenic harmone, play a key role in regulating energy metabolism, which is identical to C3adesArg derived from the cleavage of complement C3 protein by carboxypeptidase [10] is a product of innate immunity. ASP is a linking protein immunity and metabolism but recent findings have shown role of ASP in energy homeostasis and lipid metabolism [11]. ASP are responsible for stimulation of free fatty acid incorporation into adipose tissue by stimulating TG synthesis

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Table 1
Comparison of anthropometric parameters between women with obesity and women without obesity.

Anthropometric parameters	Cases (n = 260)	Controls (n = 260)	p-value
BMI	31.93 ± 1.85	23.10 ± 4.38	0.0001*
WC	89.82 ± 9.20	74.01 ± 4.38	0.0001*
WHR	0.90 ± 0.13	0.82 ± 0.06	0.0001*
SBP	132.27 ± 13.14	118.32 ± 8.89	0.0001*
DPB	83.84 ± 6.79	80.28 ± 6.65	0.0001*

Data represented in mean ± SD, *Significant.
BMI: Body Mass Index**; WC:** Waist Circumference; **WHR:** Waist Hip Ratio; **SBP:** Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure.

Table 2
Comparison of lipid profile between women with obesity and women without obesity.

Lipid profile	Cases (n = 260)	Controls (n = 260)	p-value
Serum TC (mg/dl)	169.71 ± 31.63	146.75 ± 28.24	0.0001*
Serum TG (mg/dl)	154.20 ± 45.79	107.57 ± 22.93	0.0001*
Serum HDL (mg/dl)	40.05 ± 5.65	43.55 ± 6.60	0.0001*
Serum LDL (mg/dl)	98.82 ± 30.64	81.69 ± 27.08	0.0001*

Data represented in mean ± SD, *Significant.
TC: Total Cholesterol; **TG:** Triglyceride; **HDL:** High Density Lipoprotein**; LDL:** Low Density Lipoprotein.

Table 3
Comparison of Glucose, insulin, insulin resistance, ASP and Adiponectin levels between women with obesity and women without obesity.

Biochemical parameters	Cases (n = 260)	Controls (n = 260)	p-value
FPG (mg/dl)	133.42 ± 32.27	90.56 ± 10.52	0.0001*
FPI(μU/ml)	14.11 ± 5.78	8.36 ± 5.71	0.0001*
HOMA- IR	4.91 ± 2.74	1.90 ± 1.36	0.0001*
ASP (nM/l)	25.25 ± 4.87	16.11 ± 3.83	0.0001*
Adiponectin	22.61 ± 12.95	30.67 ± 12.89	0.0001*

Data represented in mean ± SD, *Significant.
FPG: Fasting Plasma Glucose; **FPI**: Fasting plasma insulin; **HOMA-IR**: Homeostatic Model Assessment - Insulin Resistance **ASP**: Acylation Stimulating Protein.

Table 4
Correlation of ASP and adiponectin with anthropometric, clinical and biochemical parameters in women with obesity.

Parameters	ASP (r value)	p-value	Adiponectin (r value)	p-value
BMI	0.25	0.0001*	−0.07	ns
WC	0.76	0.0001*	−0.33	0.0001*
WHR	0.39	0.0001*	−0.17	0.005
SBP	0.07	ns	−0.03	ns
DBP	0.02	ns	−0.11	ns
FPG	0.95	0.0001*	−0.36	0.0001*
TC	0.38	0.0001*	−0.12	0.04
TG	0.95	0.0001*	−0.33	0.0001*
HDL	−0.55	0.0001*	0.31	0.0001*
LDL	0.21	0.0001*	−0.08	ns
FPI	0.61	0.0001*	−0.29	0.005
IR	0.80	0.0001*	−0.34	0.0001*
Adiponectin	−0.03	ns	1	
ASP	1		−0.37	0.0001*

ns: non significant, $p > 0.05$; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

through activation of diacylglycerol acyltransferase and increases glucose transport through enhanced translocation of glucose transporters and inhibition of lipoprotein lipase (LPL) activity which reduction of triglyceride lipolysis in adipocytes through inhibition of hormone sensitive lipase [12]. Adiponectin is an adipocytes specific homologue. In both human and animal studies, adiponectin are reduced in obesity and inversely correlated with diabetes and Insulin resistance [13]. The inverse relationship between obesity and plasma adiponectin level are also correlated with insulin sensitivity in healthy humans. Both ASP as well as Adiponectin activates AMPK, which mediates metabolic pathways improving glucose utilization, without increasing insulin secretion and decrease circulating NEFAs [14,15]. Hence increase level of ASP and decrease level of adiponectin may be the marker for increasing number of metabolic risk factors which is useful to identify the subject may reflect the functionality of adipose tissue.

2. Materials and method

2.1. Subject selection

In this study, total of 260 women with obesity (BMI >30kg/m2) as a study and 260 women without obesity (BMI<25kg/m2) as control were recruited. The inclusion criteria for subject consisted of women with BMI ranging of age group between 25-45 years without any metabolic and systemic diseases. Whereas, exclusion criteria for the patients who had no cardiac, respiratory, inflammatory, endocrine diseases, Pregnant, lactating and women with any kind of gynecological or obstetrical problems and on medication including hormone replacement therapy, on addictions like smoking, alcohol intake. The study was approved by the Ethics Committee of KGMU, Lucknow, U.P and the Indian Council of Medical Research, New Delhi, India **Ref. Code: 58 ECM II B/P31.** Written informed consent was obtained from all the participants completed to collect information regarding subjects' medical, personal, family, dietary, and menstrual history.

2.2. Anthropometric measurements

All subjects were evaluated for Waist Circumferences (a good marker for measuring central/visceral obesity, WC was measured midway between the margin of the lowest ribs and the iliac crest, at the point of minimal inspiration and blood pressure (BP) was measured with the Bp TRU device, 3 blood pressure readings were obtained, which uses the traditional oscillometric technique (Beckett & Goodwin, 2005).

2.3. Sample collection and biochemical estimation

Blood samples for measuring the biochemical parameters were obtained in the morning after 12 h of fast on the 10th day to rule out the hormonal variation because of menstruation, serum and plasma were separated from 6.0 ml of the blood.

2.4. Biochemical estimation

Plasma insulin concentrations were determined using immune radiometric assay (IRMA) (Immunotech Radiova, Prague). Plasma glucose concentrations were determined by glucose oxidase-peroxidase method (Merck) using semi automated glucose analyzer (Microlab 300, Merck). ASP (MYBIO.com Catalog-MBS012694) & Adiponectin (Quantikine Adiponectin, R&D system Oxford, UK) level was measured by enzyme-linked immunosorbent assay.

Insulin resistance Homeostasis model assessment (HOMA), an index of insulin resistance (IR) based on plasma levels of fasting glucose and insulin has been widely applied for quantifying insulin resistance calculated by:

HOMA -IR = [fasting Insulin (μU/l) x fasting glucose (mmol/l)/ 22.5]

2.5. Statistical analysis

All the Statistical analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA). Quantitative variables are presented as the mean ± standard deviation (SD). Comparisons between two groups were made by using Unpaired *t*-test was performed to assess the difference in biochemical parameters among the two groups. All statistical tests were two-tailed, and $p < 0.05$ was considered as statistically significant. Pearson's correlation was performed to observe the correlation of ASP and adiponectin with the metabolic risk markers.

3. Results

This is a case-control study. Total $n = 520$ female subjects, divided in to two group $n = 260$ women with obesity and $n = 260$ women without obesity.

3.1. Comparison of anthropometric parameters between women with obesity and women without obesity

The comparison of anthropometric parameters between women with obesity and women without obesity. BMI, WC,WHR, SBP DBP were significantly ($p = 0.0001$) higher among the cases compared to controls.

3.2. Comparison of lipid profile between women with obesity and women without obesity

The level of serum TC, serum TG, and serum LDL were significantly higher in women with obesity compared to women without obesity. However, HDL was significantly lower in women with obesity than women without obesity.

3.3. Comparison of glucose, insulin, insulin resistance and ASP levels between women with obesity and women without obesity

The blood glucose levels, plasma insulin level, HOMA-IR and ASP level were observed significantly higher and adiponectin level was significantly lower in women with obesity compared to women without obesity.

3.4. Correlation of ASP and adiponectin with, anthropometric clinical and biochemical parameters in women with obesity

Observation shows the correlation of ASP and adiponectin with various parameters in women with obesity. ASP was significantly positive correlated with WC ($r = 0.76$, $p = 0.0001$), glucose ($r = 0.95$, $p = 0.0001$), TG ($r = 0.95$, $p = 0.0001$), insulin ($r = 0.61$, $p = 0.0001$) and IR ($r = 0.80$, $p = 0.0001$), whereas the correlation of adiponectin was significantly negative correlated with WC ($r = -0.33$, $p = 0.0001$), glucose ($r = -0.36$, $p = 0.0001$), TG ($r = -0.33$, $p = 0.0001$), IR ($r = -0.34$, $p = 0.0001$), ASP ($r = -0.37$, $p = 0.0001$) and significantly positive correlated with HDL ($r = 0.31$, $p = 0.0001$).

4. Discussion

Adipose tissue acts as an endocrine organ that secrete a number of bioactive molecules known as 'adipokines' variation of these adipokines, plays a key role in the metabolic disorder. Present study was aimed to observe the potential role of adipocytokines, acylation stimulating protein and adiponectin with metabolic risk marker in North Indian obese women. The observation of this study shows that women with obesity have significantly higher BMI and WHR than women without obesity. Waist circumference is also significantly higher in women with obesity compared to women without obesity and concordance with other study [16]. Study shows that plasma ASP is positively whereas adiponectin is negatively correlated with waist circumference. This study concluded that waist circumference may be a better index of central obesity related to Metabolic syndrome than all the body index like as BMI, WHR in Obese women and concordance with other studies which show that increased WC is directly related with dyslipidemia and glucose intolerance in the diverse population [17,18]. These result focused that the best way to evaluate central obesity is to measure waist circumference, as the excess of abdominal fat is more strongly associated with the metabolic risk marker. Same as, women with obesity had significantly higher systolic as well as diastolic blood pressure in comparison to women without obesity consistent with another study [19]. This association shows that high BP may be responsible of elevated ASP and reduced adiponectin premature signs of endothelial dysfuction [20].

In the present study shows, higher triglyceride, total cholesterol, low density lipoprotein and lower high density lipoprotein levels were observed in women with obesity as compared to women without obesity, responsible to cause of dyslipidemia. Disturbance of lipid metabolism may have several causes, such as overweight, obesity, diabetes and physical inactivity which could be an key factor of metabolic syndrome. These findings of the study are consistent with another study of our group [21,22].

The observation of study, raise plasma glucose, insulin levels and the value of insulin resistance were found in women with obesity suggesting the presence of insulin resistance in obese women. Insulin hormone regulates almost all aspects of adipose tissue functioning. Insulin are responsible to the uptake of fatty acids by stimulation of enzyme lipoprotein lipase. Evidence following the fact that by the time fasting hyperglycemia or glucose intolerance set in considerable β-cell destruction might be already occurred [23]. The observations of this study are also in agreement with the studies that reveal a high level of circulating ASP and low level of adiponectin strongly associated with obesity all risk factors for cardiovascular disease.

ASP and Adiponectin are important counterparts in the regulatory system of energy homeostasis in humans, though it remains unclear whether they are linked to each other while their elevate level of ASP and lower level of adiponectin in adipose tissue are responsible for diabetes and cardiovascular disease that are associated with obesity and metabolic disorder [7,12,24,25]. Present study significantly higher circulating plasma level of ASP and lower level of adiponectin in study group than in control group and was correlated with increase mass of fat cell [19] Several studies suggests that the high serum concentration of ASP and low concentration of adiponectin in obesity, leads to the development of metabolic syndrome [26,27]. *In vivo* and *in vitro* studies have demonstrated that ASP function in promoted triglyceride clearance to elevate fatty acid trapping and fat storage in adipose tissue [27,28]. The functional receptor of ASP is C5L2 [29] and variation in this receptor reduces ASP binding is associated with increased ASP levels and adiponectin enhances insulin sensitivity, increases fatty acid oxidation, glucose uptake and suppresses hepatic glucose production [30,31]. These studies strongly indicate these factors usually related to, diabetes, metabolic disorders and cardiovascular disease. Thus, obesity is the main determinant of metabolic risk marker due to increases level of plasma ASP and decrease level of adiponectin. In conclusively, study show that the inverse relationship of these adipokines: increase level of ASP and decrease level of adiponectin play an important role in energy metabolism and lead to obesity and its related disorders with metabolic risk markers in North Indian obese women with metabolic syndrome Moreover

further studies are required to find the pathological role of ASP and adiponectin in North Indian obese women with metabolic syndrome.

Conflicts of interest

There is no conflict of interest and no financial disclosure.

Source of funding

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.dsx.2018.07.017.

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