Research article

Circulating NAMPT/ PBEF /Visfatin and its cardiometabolic risk in young obese adults

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(Received: January 2022 Revised: May 2022 Accepted: June 2022)

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ABSTRACT

Introduction and Aim: In this era of obesity pandemic, obesity related metabolic derangements has demanded more clinical attention due to its high rate of morbidity and mortality. Altered lipid profile and atherogenicity have increased the cardio metabolic risks, even in young adults and adolescents. Among various adipocytokines, visfatin/PBEF(pre-B-cell colony-enhancing factor)/NAMPT (nicotinamide phosphoribosyl transferase), predominantly secreted from the visceral fat, helps to predict the amount of fat that has a strong correlation with the derangement of cardio metabolic profile compared to the subcutaneous fat.The aim of this study is to determine the serum PBEF/visfatin levels in young obese, and to evaluate its correlation with body fat distribution, lipid parameters and the atherogenic index.

Materials and Methods: The subjects were 60 young obese adults in the age group of 18-35 years and age and sex matched 30 controls. Serum visfatin, lipid parameters and anthropometric indices- weight, height, HC (Hip circumference)and WC(waist circumference) were measured and BMI (Body mass index),WHR(waist–hip ratio) andatherogenic index (log of TG/ HDL-C) was calculated.

Results: NAMPT/PBEF/Serum visfatin levels, BMI, WC, WHR, TG, LDL-C was significantly higher in young obese subjects than the controls ($P< 0.05$). The AIP - atherogenic index of plasma was also significantly higher in young obese with P value < 0.01. There was positive correlation of TG, LDL-C and atherogenic index with serum NAMPT/visfatin levels. BMI also showed a significant positive correlation with r value of 0.56 ($P= 0.01$).

Conclusion: These results highlight that serum NAMPT/visfatin levels, due to its association with the atherogenic index, as a significant marker for assessing the cardio-metabolic risks in obese subjects. Higher atherogenic index of plasma in obese individuals focuses the impact of visceral fat in the initiation of atherosclerotic plaques even at a younger age group.

Keywords: NAMPT/PBEF/visfatin; atherogenic index; visceral fat; cardio metabolic risk.

INTRODUCTION

The prevalence of obesity is continuing to increase worldwide, affecting all age groups and has become the leading cause of death (1,2) due to its inevitable association with metabolic disorders like hypertension, diabetes, dyslipidemia, cardiovascular disorders, non-alcoholic fatty liver disease (NAFLD) and also certain cancerous conditions (3).A statistical report by WHO shows, 1 in 6 adults are obese worldwide and about 2.8 million die every year with overweight and metabolic disorders associated with obesity. In India, 213 million people are obese- 45.6% in urban and 22.5% in rural areas (4).

The factor that makes the adipose tissue a lethal organ is the adipocytokines it secrets, which alters the metabolic homeostasis increasing the incidence of cardiometabolic diseases in obese population (5,6). A relatively newer multifaceted adipocytokine, visfatin/NAMPT, is also found in bone marrow, skeletal muscle, liver and lymphocytes though principally secreted in visceral adipose tissue. Visfatin/NAMPT is also identified as a growth factor, pre B cell colony enhancing factor- 1 (PBEF1) in the lymphocytes that enhances the differentiation of stem cells to pre B cells (7,8). It is also identified as an intracellular enzyme, nicotinamide-5-phospho ribosyl -1-pyrophosphate transferase (NAMPT), which catalyses the rate limiting step in nicotinamide dinucleotide (NAD) synthesis (9).The interesting fact is that NAMPT is also found to be a potent proinflammatory mediator that participates in various inflammatory conditions. Obviously, inflammation of adipose tissue that induces insulin resistance and metabolic syndrome becomes the fundamental cause for the co-morbidities, related to obesity (10).

Dyslipidaemia, being the major metabolic derangement of obesity becomes the cause for the deposition of fat in the sub-endothelium of blood vessels that leads to atherosclerosis (11). Researchers have proved thatAtherogenic Index of plasmaas a significant predictor of atherosclerosis and

dyslipidemia which can be calculated using the formula log TG/HDL (12).

There are two types of adipose tissue in humans, brown adipose tissue (BAT) and white adipose tissue (WAT). BAT is mainly involved in non-shivering thermogenesis, by which heat is produced by uncoupling of oxidative phosphorylation in mitochondria. WAT is the form of fat in which triglycerides is stored. White adipose tissue can be further divided as subcutaneous and abdominal depots, both of which have distinct physiological roles (13).

Visceral fat, the abdominal fat surrounding the viscera, have a strong association in the metabolic derangement than subcutaneous fat. Hence the body fat distribution plays a significant role in the pathogenesis of the metabolic disorders associated in obesity(14). Though many authors have found positive association between visfatin and BMI and body fat index, there is lack of studies stating the association of visfatin and atherogenic index . So in this study we tried to explore how far is the correlation of visfatin with the atherogenic index in young obese population that would relatively predict the cardiometabolic risks at an earlier stage.

METHODS

This prospective study involves 60 young obese subjects (BMI ≥ 25 kg/m² - Asian cut off) and 30 non obese controls(BMI≤ 24.9 kg/m²).Exclusion of those subjects with co-morbidities - like Hypertension,Diabetes,Hypothyroidism, and Pregnant women, women on Oral Contraceptive Pills were done.The study was conducted in compliance with Helsinki declaration 1964and its amendments, after approvalfrom institutional ethical committee.

All subjects were subjected to detailed history taking and clinical examination after informed written consentWeight, Height, HC (Hip circumference) and WC (waist circumference) were measured and BMI (Body mass index) ,WHR(waist–hip ratio) was calculated. Body weight and height was measured and BMI was calculated. Waist circumference (WC), hip circumference (HC), was measured and waist-hip ratio (WHR) calculated.

After overnight fasting, six ml of blood was collected by phlebotomy in the morning, serum separated immediately and serum aliquots frozen (-80°C) on the same day, and stored until further analysis.TC (Total cholesterol), HDL-C (High-Density Lipoprotein-Cholesterol), LDL-C (Low-Density Lipoprotein-Cholesterol), and Triglycerides were determined by enzymatic procedure using the commercially available test kit (Diasys, Connecticut, United States). Very Low-Density Lipoprotein –C, was calculated using the formula, (TGL / 5). Theatherogenic index of Plasma was calculated using the formula log TG/ HDL-C.

Serum concentrations of visfatin were assayed using a commercial ELISA kit (Bioaim Scientific Inc, Ontario, Canada) with a lowerlimit of sensitivity of 0.11 ng/ml and intra assay and interassaycoefficients of variations of <15% and <10%, respectively.The kit showed no cross-reactivity with any other cytokines tested.

Statistical analysis

The normal distribution of continuous variables was done using Kolmogrov-Smirnov and Shapiro –Wilk test. Student 't' test was done to test the significant difference in means of the study and the control group. Significant differencefor all the statistical tests, were determined by P value of <0.05. Pearson correlation was done for studying the correlation between variables.

RESULTS

After selection of age and sex matched controls, the mean age of the cases (young obese adults) was 31.75± 3.9 and that of controls (nonobese) were 31.26±3.4. (Table 1).

Table 1: Baseline characteristics

Parameters	**Obese**	**Control**	**P**
Age	31.75 ± 3.9	31.26± 3.4	NS
Weight	80.0 ± 13.0	59.07± 7.1	0.01
Height	160.40± 7.3	163.60 ± 6.2	0.011
BMI	31.08± 3.6	22.22 ± 1.7	0.001
Waist circumference(cm)	99.38 ± 5.2	74.40 ± 2.5	0.001
Hip circumference (cm)	106.97± 3.0	87.53 ± 2.9	0.01
Waist - Hip ratio	0.927± 0.098	0.845± 0.039	0.001

NS =not significant

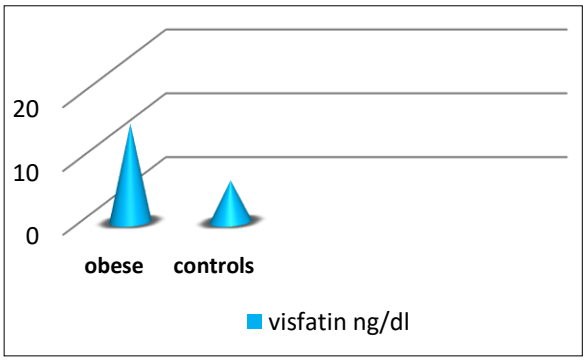

Fig. 1: Distribution of visfatin among the study population

Mean serum NAMPT/visfatin levels were higher in the young obese (15.6±2.0 ng/dl) than the controls (6.7±0.9ng/dl) with significant p value of 0.00 (Fig.1). Means of Weight, BMI, WC, HCand waist-hip ratio were significantly higher in the obese subjects than the controls group, whereas the mean height was higher in controls than the study population, with a significant P:< 0.05.(Table 1; Fig 2).

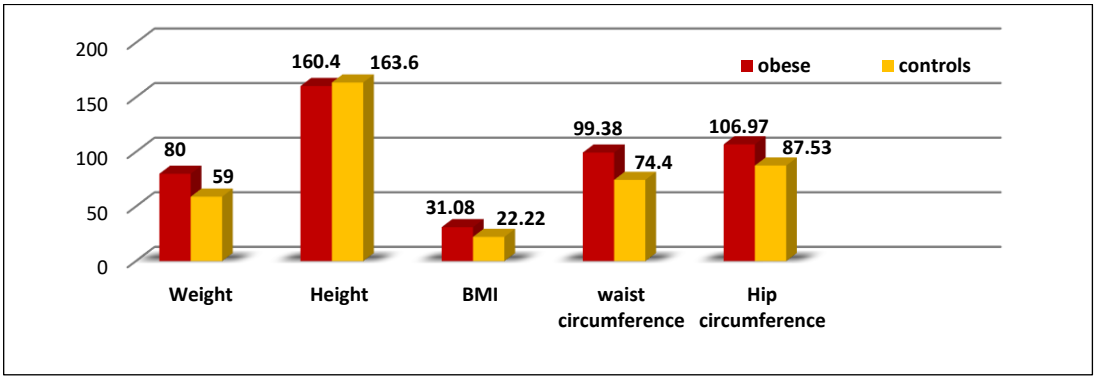

Fig. 2: Distribution of anthropometric indices among the study population

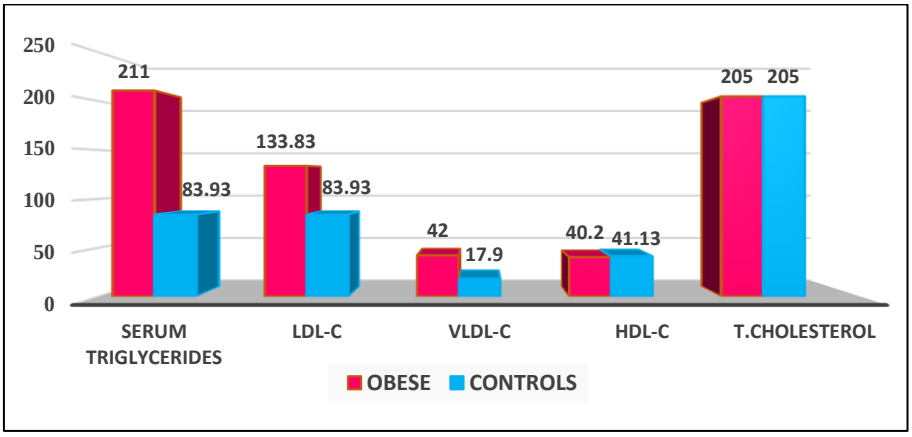

Fig. 3: Lipid profile in the study population

Table 2: Correlation of serum visfatin with various parameters in obese subjects

Parameters	r value	P value
BMI	0.926	0.00
Waist circumference	0.725	0.00
Hip circumference	0.106	NS
Waist –Hip Ratio	0.659	0.00
Triglycerides	0.32	0.04
LDL-C	0.911	0.00
Atherogenic index	0.599	0.00

Obese study subjects had higher mean serum triglycerides, LDL-C, and VLDL-C than the controls. The HDL-C was lower in the obese subjects than the controls. Total cholesterol levels were equal in both the study groups(Fig. 3).

The young obese study group have significantly higher atherogenic index than controls ($P < 0.016$). Serum visfatin/PBEF levels in the obese subjects was positively correlated with BMI (r: 0.926), WC (r: 0.725), WHR (r: 0.659), TG (r: 0.32), LDL-C (r: 0.911) with P value<0.05 and insignificant correlation with hip circumference (Table 2).

As with correlation studies in the study group, PBEF/visfatin had positive correlation with atherogenic index (Fig. 5), BMI and atherogenic index also had positive correlation (r: 0.567 P:0.01; Table 2).

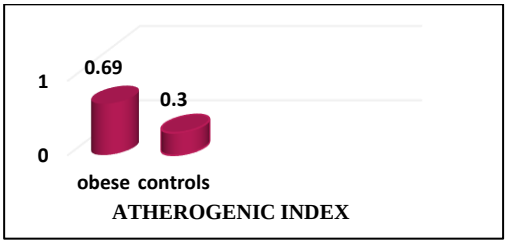

Fig. 4: Atherogenic index in the study population

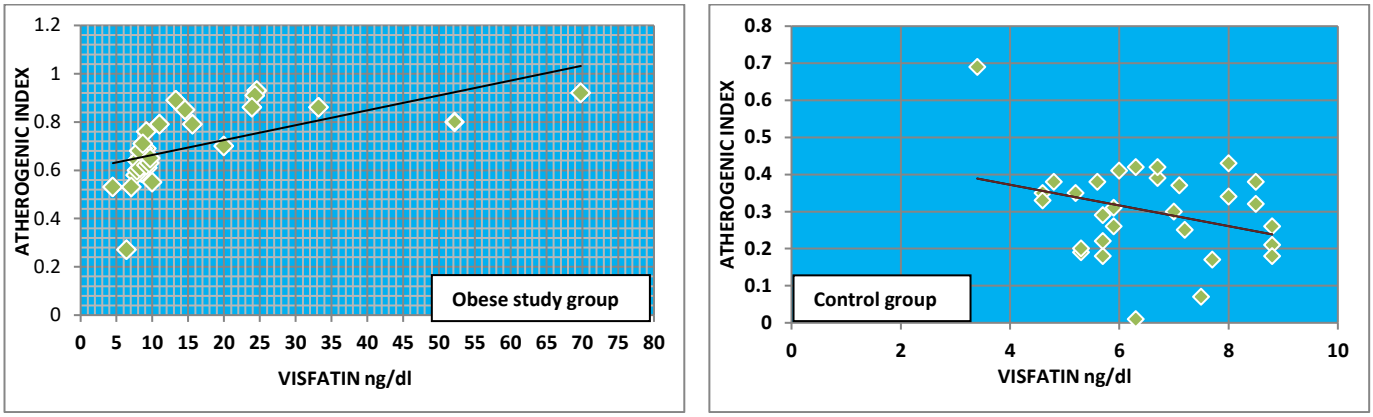

Fig. 5: Scatter plot - correlation between visfatin and atherogenic index
The obese study group showed an inverse correlation of serum visfatin with HDL-C (r: 0.568).

DISCUSSION

We designed this study to determine the serum PBEF/visfatin in young obese adults and to demonstrate its correlation with the atherogenic index. We determined the mean age of the study population to be 31.34 ±5.0 with 51% males and 49% females. In this study, it was seen that the serum levels of PBEF/visfatin was higher in young obese adults than the non-obese controls that were in accordance with reports of Kaminska *et al.*, (15) in adults and there was a positive correlation between serum visfatin levels and adiposity in adolescents, according to Tuskasen *et al.*,(16). Regarding the anthropometric indices, the BMI and WHR was higher in obese young adultsin this studyand they had positive correlation with the serum visfatin levels which were in consistent to the findings of Davutoglu *et al.*,(17) and Berndt *et al.*, (18).

With lipid profile, we had positive correlation of serum Triglycerides and LDL-C with visfatin, in this study and this points to an insulin-mimetic property of visfatin that have profound effects on lipid homeostasis and triglyceride metabolism.

In our study the atherogenic index was significantly higher in young obese and had positive correlation with serum visfatin with r: 0.599 (P<0.00). BMI and the Atherogenic index also had a positive correlation in obese study group (r value: 0.568 p:0.01).

Dobiasova *et al.*,(19) pointed AIP to be the significant predictor of cardiovascular risk for both research and for practice. Simões *et al.*, (20) also demonstrated the atherogenic index of plasma as the best marker of atherosclerosis in their studies.

As NAMPT/visfatin being produced from various cells like monocytes, lymphocytes, neutrophils and hepatocytes apart from visceral fat, it has a significant association with various inflammatory markers that cause endothelial dysfunction (21). Moreover, Wang *et al.*, have stated that visfatin causes smooth muscle cell proliferation through NAMPT- dependent mechanism. (22).

Thus visfatin/Nampt enhance the production of proinflammatory cytokines, activate leucocytes and synthesize various adhesion molecules those accounts together for the atherosclerotic plaque formation (23). Zheng *et al.*, (24) in their study have proved visfatin is closely associated with atherosclerotic plague in carotid arteries of type 2 diabetic patients. Also authors have given scientific evidences that visfatin causes destabilization of atherosclerotic plagues. (25). Hence Zheng *et al* have rightly stated visfatin to be the clinical marker of cardiovascular diseases.

CONCLUSION

From this study we infer that high PBEF/Visfatin, correlating with high atherogenic index in young obese adults will subsequently cause endothelial dysfunction of bloodvessels and enhance cardiometabolic risks. So we suggest that PBEF/Visfatin/NAMPT can be targeted in pharmacological research with the scope of preventing cardiovascular complications at an earlier stage.

ACKNOWLEDGEMENT

We extend our sincere thanks to all patients participated in this study

CONFLICT OF INTEREST

The authors have no conflict of interests to declare that are relevant to the content of this article.

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