Original Research Article

Association of BMI with markers of angiogenesis in healthy population

Shivani Jaswal*, Harjeet Kaur, Jasbinder Kaur, Seema Gupta

Department of Biochemistry, Government Medical College and Hospital, Chandigarh, India

*Correspondence:
Dr. Shivani Jaswal,
E-mail: shivanirishiraj@yahoo.co.in

ABSTRACT

Background: Obesity is associated with an increased risk of atherosclerosis, which can be mediated by an increase in angiogenesis and inflammation. The objective of the present study was to explore the relationship between BMI and levels of VEGF, a circulating biomarker of angiogenesis.

Methods: 225 healthy volunteers in the age group of >18 years formed the subjects of the study. Individuals with any acute or chronic illness including history of HT, DM, and smoking, alcohol or drug abuse or on any long term medication were excluded from the study. Anthropometric measurements were taken, and BMI calculated. Blood samples were taken, and serum levels of VEGF were estimated using commercially available ELISA kits. Student's 't' test was done for comparison and correlation was assessed using Pearson's method.

Results: A statistically significant difference in the levels of VEGF was found in subjects with BMI < 25 kg/m2 as compared to subjects with BMI > 25 kg/m2 ($p<0.001$). A significant positive correlation was found between the levels of VEGF and BMI in both males and female subjects of the study group (r=0.68 and 0.73 respectively).

Conclusions: The positive correlation of levels of VEGF with BMI in the healthy subjects of the study group may be related to the expansion of adipose tissue and to the concomitant formation of new vessels to support tissue deposition. These factors may predispose an individual to an increased risk of atherosclerotic damage later in life. VEGF may therefore, have a potential as a biomarker for the prediction of cardiovascular risk and estimation may allow intervening with lifestyle modifications and nutritional changes before the disease is manifested and pharmacotherapy is required.

Keywords: BMI, Cardiovascular risk, Obesity, VEGF

INTRODUCTION

WHO has recognized obesity to be one of the most common, yet among the most neglected, public health problem in both the developed and the developing countries.[1] World health statistics report 2012, states that one in six adults is obese and nearly 2.8 million individuals die each year due to overweight or obesity.[2] Obesity is thus, now being recognized as a disease in its own right. Studies have strongly associated obesity with other metabolic disorders including DM, HT, dyslipidemia etc.[3,4,5] The association between obesity and cardiovascular risk could be attributed to the increased risk of atherosclerosis in obesity mediated by an increase in angiogenesis and inflammation.[6] Establishing biomarkers which may allow detection of high risk cases of atherosclerosis at an early stage would be beneficial as it would allow intervention with lifestyle and nutritional changes before the disease is manifested.

Vascular endothelial growth factor (VEGF), is one such angiogenic marker which is produced by the adipose tissue and has been shown to have a statistical dependence on body mass index (BMI) in overweight and obese individuals.[7]

The present study was thus, planned to explore the association between VEGF, a circulating biomarker of angiogenesis and BMI in healthy individuals.

METHODS

The present study was conducted in the Department of Biochemistry of a tertiary care hospital in the northern part of India. The study was designed as a cross-sectional study. 225 healthy volunteers from the hospital staff and patient attendants aged more than 18 years formed the subjects of the study. Individuals with any acute or chronic illness including history of HT, DM, and smoking, alcohol or drug abuse or on any long term medication were excluded. The study was conducted with financial grant from the Department of Science & Technology, Chandigarh Administration, Government of India. Clearance from the Institutional Research and Ethics Committee was obtained and informed consent was taken from all the participants of the study prior to enrolment. All participants underwent anthropometric measurements and BMI was calculated. The subjects were divided into 4 categories depending on the BMI as per the criteria for Asian population.[8]

Blood samples were drawn from all participants at the time of recruitment. Apart from the routine investigations, serum levels of VEGF were estimated using commercially available ELISA kits, according to manufacturer's instructions.

The results were expressed as mean±SD and statistical comparison was done using student's "t" test. Pearson's coefficient was used for correlation analysis. The difference was considered significant when $p < 0.05$.

RESULTS

The study was conducted on 225 healthy volunteers in the age group of more than 18 years of age. The demographic characteristics of the study population are given in Table 1.

Table 1: Basic characteristics of the participants of the study.

	Underweight	Normal healthy	Overweight	Obese	P-value
N	17	74	89	46	
Age (years)	31.9±10.9	30.9±11.1	34.9±12.10	43.3±10.6	
BMI (kg/m^2)	17.5±0.86	21.4±1.2	24.8±1.04	31.0±4.2	<0.001
VEGF (pg/ml)	21.04±1.89	28.4±15.3	49.8±38.3	106.8±65.4	<0.001

The mean age of the subjects of the study group was found to be 35.3±12.1 years. The subjects were divided into underweight, normal weight, overweight and obese according to the BMI. No significant difference was found in the age of the subjects of the different groups. However, a positive correlation was found between age and BMI in the subjects of the study.
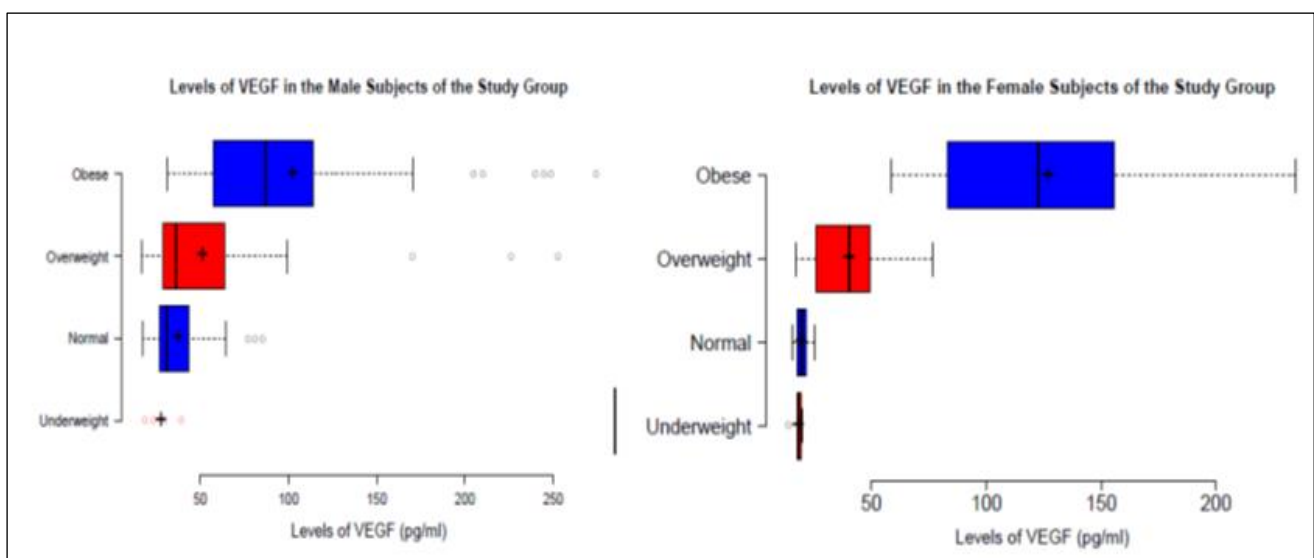

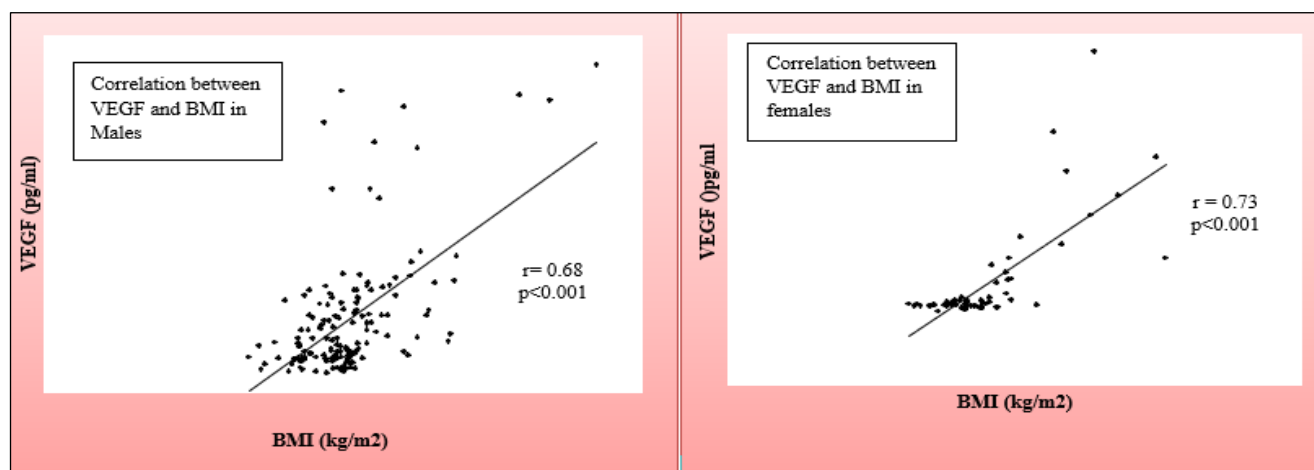**Figure 1: Levels of VEGF in the subjects of the study group.**

Figure 2: Correlation between levels of VEGF and BMI in the subjects of the study group.

The mean level of VEGF in the subjects of the study group was found to be 53.4±49.3pg/ml. When the subjects of different BMI groups were compared, it was found that the groups differed significantly showing a trend for lower VEGF concentrations in normal weight (28.4±15.3pg/ml) than in overweight (49.8±38.3 pg/ml) and also lower in overweight as compared to obese (106.8±65.4 pg.ml). A similar difference in levels of VEGF among the various BMI groups was found in both the male as well as the female subjects of the study group (Figure 1).

When the levels of VEGF were correlated with the respective BMI in the subjects of the study group, a significant positive correlation was found in both male (r=0.68, p<0.001) and female subjects of the study group (r=0.73, p<0.001) (Figure 2).

DISCUSSION

The prevalence of obesity has been increasing worldwide in adults and children.[9,10] Moderate to severe obesity has been found to be an important risk factor for heart disease, directly or indirectly through intervening risk factors, such as hypertension, dyslipidemia, and diabetes. Many large scale studies have shown a positive relationship between CVD mortality and BMI.[11,12]

Adipose tissue until recent times was considered simply as a storage site for excess fat, but off late it has been appreciating to be a site of synthesis and release of cytokines and adipokines, which not only act locally both in a paracrine or autocrine manner, but also have endocrine function. Some of these cytokines have effects on endothelial cells and have angiogenic activity.[13]

Endothelial cells are abundant in adipose tissue and an expression of the capillary bed appears to be necessary for the development of obesity.[14] It has been shown that antiangiogenic therapy is accompanied by remodelling of adipose tissue capillary beds and a reduction in fat mass in rodents suggesting the role of angiogenesis in obesity.[13,15]

Adipose tissue contains abundant endothelial cells, which secrete both angiogenic factors, such as vascular endothelial growth factor (VEGF), and antiangiogenic factors such as angiostatin and endostatin.[13]

Angiogenesis is a result of a balance between angiogenic factors and factors which stimulate endothelial cell proliferation and migration and antiangiogenic factors which inhibit these processes. These angiogenic factors may have autocrine or paracrine function and apart from local effects on the adipose tissue, they may have effects in other capillary beds and contribute to endothelial dysfunction and cardiovascular disease, both of which have been linked to obesity.[16]

VEGF family of proteins is important for development of blood vessels during embryogenesis and in pathological conditions like tumorigenesis.[17] VEGF is a heparin-binding glycoprotein with angiogenic, mitogenic and vascular permeability enhancing activities specific for endothelial cells.[18]

Serum VEGF levels have been found to be positively correlated with BMI and visceral fat mass in a group of overweight and obese individuals, but there are very few data on its association with BMI in healthy individuals.[13,19]

The results of the present study have shown increased levels of VEGF and a positive correlation between the levels of VEGF and BMI in healthy individuals. The findings provide a reliable understanding of the problem, which may aid in the design of new and better interventions to ameliorate the epidemic of obesity. The

results also support the imperative to redouble efforts to assist in increasing healthy behaviours.

CONCLUSION

The positive correlation of levels of VEGF with BMI in the healthy subjects of the study group may be related to the expansion of adipose tissue and to the concomitant formation of new vessels to support tissue deposition. These factors may predispose an individual to an increased risk of atherosclerotic damage later in life. VEGF may therefore, have a potential as a biomarker for the prediction of cardiovascular risk and estimation may allow intervening with lifestyle modifications and nutritional changes in high risk cases before the disease is manifested and pharmacotherapy is required.

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