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Original Article

Physiology Section

Influence of BMI on Cardiac Output and Peripheral Blood Flow in Young Adult Males

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ABSTRACT

Introduction: Obesity is increasing at an alarming rate in young population which has a direct effect on their cardiovascular health resulting in development of hypertension, dyslipidaemia and peripheral vascular diseases at an early stage of life.

Aim: To determine association of BMI with cardiac output and peripheral blood flow in young adult males.

Materials and Methods: The study was a cross-sectional study done in Department of Physiology, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India, between August to September 2015 under ICMR STS project. A total of 90 males with age 17-25 years with no history of smoking, alcoholism, diabetes mellitus, hypertension, cardiovascular or respiratory diseases were enrolled. BMI (kg/m^2) was calculated and equal numbers of subjects were categorised into three groups according to BMI (South Asian Standards).

Non obese (BMI <22.9 kg/m^2), Overweight (BMI between 23-24.9 kg/m^2) and Obese (BMI ≥25 kg/m^2). Cardiac output and peripheral blood flow of forearm and calf were measured using Non Invasive Continuous Cardiac Output and Peripheral Blood Flow Monitor (NIVOMON) series. The data were analysed statistically by using one-way ANOVA test.

Results: Cardiac output was significantly more in obese group compared to overweight and normal BMI group (5.7±0.43 vs. 5.26±0.54 vs. 4.95±0.65 L/min, p<0.01). Forearm and calf blood flow of both limbs were significantly less in obese group compared to overweight and normal (p<0.01).

Conclusion: Obese subjects have increased cardiac output which may lead to cardiac complications like left ventricular hypertrophy and high output cardiac failure in future. Inspite of increased cardiac output, peripheral blood flow was decreased in obese subjects which may be due to endothelial dysfunction and accelerated atherosclerotic vasoconstriction which may result in peripheral artery disease in future.

Keywords: High output failure, Obesity, Peripheral artery disease

INTRODUCTION

Obesity is rising as an epidemic globally including India and according to WHO, one in six people on Earth (approximately one billion) are overweight and, alarmingly, more than 300 million of them are obese. This might be due to more sedentary life style and excessive intake of energy rich diet and is associated with various chronic diseases such as hypertension, metabolic syndrome, dyslipidaemia, type 2 diabetes mellitus, and Cardiovascular Diseases (CVD) and thus pose a major public health problem [1,2].

Incidence of heart diseases has increased dramatically in younger age group. Coronary Artery Disease (CAD) is affecting Indians 5-10 years earlier than other races. Indians also show higher incidence of hospitalisation, morbidity, and mortality than other ethnic groups due to CVD [3].

The haemodynamic consequences of obesity are increased stroke volume and heart rate and hence, it leads to an increase in cardiac output in obese people. The compensatory adaptation of the hyperdynamic circulation results in dilatation of left ventricular chamber to accommodate the increased venous return and, in turn, development of an eccentric type of hypertrophy to keep the wall stress normal [4]. This results in increase in Blood Pressure (BP) in obese individuals. BP measured in young and middle-aged adults is positively related to risk of CAD in older age. This implies that the risk of CVD starts at a young age. A study done in University of Glasgow Student also revealed that BPs in normotensive males at a mean age of 20.5 years predicted future CVD [5].

In extreme obesity, this condition can progress to non ischaemic dilated cardiomyopathy and contractile dysfunction [6,7]. Obesity is also associated with endothelial dysfunction, which is an initial step in the pathogenesis of atherosclerosis and strongly linked to cardiovascular mortality [8].

Irrespective of gender, religion, or social class Asian Indians worldwide showed a prevalence of CAD of 50-400% higher than people of other ethnic origin. CAD has spread as an epidemic in India with a 4-fold increase in prevalence in urban Indians compared to Americans. On comparing, the incidence of CAD rates between West and India over the past 30 years, the CAD rates have halved in the West, but in India the rates have been doubled. The average age of first Myocardial Infarction (MI) has decreased by 20 years in India. About half of all MI cases in Asian Indian males, occur below 50 years of age. These trends of increased incidence of early CAD in Asian Indians can be attributed to genetic susceptibility, resulting from increased lipoprotein (a) levels, which are due to changes in lifestyle in the form of changes in diet and urbanisation. Considering any series of single or combination of risk factor(s), Asian Indians show CAD rates double that of Whites [9].

Peripheral vessels consist of arteries and veins supplying the skeletal muscles of arms and legs i.e., blood vessels distant from heart. Blood flow to arms and legs constitutes the peripheral blood flow. Blood flow to skeletal muscles of limbs is important as these have locomotory functions which help us in daily activities. Any compromise in peripheral blood supply will cause painful cramping, fatigue, intermittent claudication and peripheral vascular disease [10].

The NIVOMON series is a non invasive instrument which works on the principle of impedance plethysmography to measure cardiac output and peripheral Blood Flow Index (BFI) [11]. The normal cardiac output being 4-8 L/minutes [12]; the normal peripheral BFI of forearm and calf being 0.8±0.16 and 0.76±0.13, respectively [13].

The present study was designed to find the association of cardiac output and peripheral blood flow with BMI in healthy young adult male.

MATERIALS AND METHODS

The present study was a cross-sectional study designed to investigate the association of obesity with cardiac output and peripheral blood flow. The study was done in Department of Physiology, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India, between August to September 2015 under Indian Council of Medical Research (ICMR) Short Term Studentship (STS) project. Ethical clearance was obtained from the Institutional Ethical Committee and written informed consent was obtained from all subjects. Male students with age between 17-25 years were included in the study. Subjects who were smokers and alcoholics and who were suffering from diabetes mellitus, hypertension, and any other cardiovascular or respiratory diseases were excluded from the study.

Classification of Subjects into Groups

All the male students of I, II and III year MBBS (152) were enrolled in the study after taking written informed consent and considering the inclusion and exclusion criteria.

The body weight was measured in kilogram (kg) by a mechanical scale to the nearest kg. Height was measured to the nearest one centimeter (cm). Body Mass Index (BMI) (kg/m^2) was calculated by the Quetelet's formula: weight/height^2 (kg/m^2).

It was a pilot study done under STS ICMR project. So, out of 152 subjects, 30 subjects each were selected randomly in three groups according to BMI (South Asian Standards) [12]:

Group A: Non obese (BMI <22.9 kg/m^2),

Group B: Overweight (BMI between 23-24.9 kg/m^2) and

Group C: Obese (BMI ≥25 kg/m^2)

Method of measuring cardiac output and peripheral blood flow:

Cardiac output and peripheral blood flow were measured using NIVOMON series (Larsen and Toubro Ltd., India) [11].

Cardiac output was measured using eight colour coded leads given in NIVOMON series whose location is given in [Table/Fig-1].

The NIVOMON works on the principle of impedance plethysmography, as the blood flow through the aorta determines most of the changes in the impedance; it is possible to compute the main blood flow in the aorta from these changes over a period of time.

For studying peripheral blood flow, impedance plethysmogram will be recorded from forearm and calves of both sides of the subjects, and the lead placement of which is given in [Table/Fig-2].

STATISTICAL ANALYSIS

Descriptive data were presented as mean±standard deviation and one-way ANOVA was used to compare BMI with cardiac output and peripheral blood flow. The mean difference was defined as significant at p<0.05 level. SPSS version 20.0 was used to analyse the data.

Lead colour	Lead location on the subject
Red (I1 and I1')	Behind the ears (Top pair)
Yellow (V1 and V1')	Roof of the neck (Second pair)
Violet (V2 and V2')	Level of xiphisternum (Third pair)
Green (I2 and I2')	End of ribcage or >5 cm from third pair (Bottom pair)

[Table/Fig-1]: Electrode placement for measuring cardiac output.

Location	I1	I2	V1	V2
Forearm	Forehead	Feet	Below elbow	Above wrist
Calf	Forehead	Feet	Proximal calf	10-15 cm distal to V1

[Table/Fig-2]: Electrode placement for measuring peripheral blood flow (forearm and calf).

RESULTS

The mean age of the subjects was 19.7±2.18 years. The mean BMI of the three groups is shown in [Table/Fig-3].

BMI categories	Normal BMI (n=30)	Overweight (n=30)	Obese (n=30)
Mean±SD (kg/m^2)	20.54±1.52	23.83±0.56	27.33±2.88

[Table/Fig-3]: Mean BMI of 3 categories of BMI.

One-way ANOVA was done to compare BMI with cardiac output, forearm and calf blood flow of both the limbs. When difference was found, Bonferroni test was used.

The mean cardiac output was significantly more in obese group in contrast to overweight and normal BMI group. The mean cardiac output of overweight group was more than normal group but the result was not statistically significant [Table/Fig-4].

Similarly, the mean BFI of right forearm was significantly less in obese group in contrast to overweight and normal BMI group. The mean BFI of overweight group was less than normal group but the result was not statistically significant [Table/Fig-4].

BMI	Normal (n=30) Mean±SD	Overweight (n=30) Mean±SD	Obese (n=30) Mean±SD	ANOVA (F-value)	Post-hoc (Bonferroni) (p-value)
Cardiac output (L/minute)	4.95±0.65	5.26±0.54	5.7±0.43	13.89	N vs Overwt: p=ns N vs obese: p<0.001 Overwt vs obese: p=0.008
Right forearm BFI	0.85±0.17	0.70±0.32	0.43±.19	p<0.001	N vs Overwt: p=ns N vs obese: p<0.01 Overwt vs obese: p<0.01
Left forearm BFI	0.88±0.17	0.69±0.20	0.47±0.37	23.36	N vs Overwt: p=0.017 N vs obese: p<0.01 Overwt vs obese: p=.006
Right calf BFI	0.83±0.18	0.73±0.18	0.47±0.19	p<0.001	N vs Overwt: p=ns N vs obese: p<0.01 Overwt vs obese: p<0.01
Left calf BFI	0.79±0.25	0.72±0.16	0.44±0.18	18.36	N vs Overwt: p=ns N vs obese: p<0.01 Overwt vs obese: p<0.01

[Table/Fig-4]: ANOVA comparing BMI with cardiac output and peripheral blood flow.
BFI: Blood flow index
N: Normal BMI
Overwt: Overweight
NS: not significant

DISCUSSION

The present study aimed to determine the association of BMI and cardiac output, forearm and calf blood flow in healthy young male adults. Present results were consistent with our hypothesis.

Cardiac output was found to be significantly more in obese subjects compared to overweight and normal BMI group. Similar results were found in other studies too [13-15]. Obese individuals have expanded central blood volume. In addition, stroke volume and cardiac output are both increased. One of the reasons for this elevation in blood volume and cardiac output may be a rise in metabolic demand in both lean and fat masses. Another reason may be production of a low resistance vascular circuit by fat depots in obese that may further result in rise of cardiac output. Changes in renal absorption of salt and water may also occur. All these factors

together give rise to volume overload which can result in high output failure in future [14].

Another study revealed that obese patients demonstrated elevated cardiac output, which is associated with an expanded intravascular (i.e., plasma and total blood) volume. Cardiac output in obesity parallels the expansion of total blood volume, and both seem to reflect the increase in metabolic requirements by additional (adipose tissue) body mass [13].

In contrast to present study, another study done by Collis T et al., showed that free fatty mass is more importantly related to cardiac output and stroke volume as compared to adipose tissue mass. Free fatty mass (comprising organ cell mass and non fatty tissues, including tendons, ligaments, and bone) represents metabolically active tissue; up to 99% of body metabolism takes place in the body cell mass. Given that cardiac output is known to be intimately related to the level of metabolism, through tissue demands for oxygen, free fatty mass is more correlated with cardiac output [15].

The present study showed both right and left forearm blood flow was significantly less in obese subjects compared to overweight and normal BMI group; whereas, in contrast to right forearm, there was significant association in blood flow of left forearm between overweight and normal BMI group. As majority of the subjects in the present study were right handed, the blood flow to the active limb was more.

These findings are also comparable to other studies done in India and abroad [13,16,17].

Similar to present study, another research showed negative correlation between BMI and BFI of upper limbs and lower limbs [17]. Studies have shown forearm vascular conductance at rest was inversely associated to BMI. Obese children had lower forearm vascular conductance than lean children at rest and this difference was abolished after intervention therapy with diet and physical training [16,17].

From the results, it is evident that inspite of increased cardiac output, the peripheral blood to limbs have decreased. This can be explained by reasons discussed vide infra.

Excess weight gain is associated with increased sympathetic nervous system activation by hyperleptinaemia, activation of the central pro-opiomelanocortin/melanocortin-4 receptor, hyperinsulinaemia/insulin resistance, hypoadiponectinaemia, hypoghrelinaemia, increased angiotensin II levels, and baroreceptor dysfunction. This result in vascular hypertrophy and rarefaction of skeletal muscle vascularisation, which may lead to structural changes that will decrease the blood flow in peripheral tissues [18].

Increased vascular resistance, decreased vasodilation and decrease in blood flow may be attributed to sympathetic neural hyperactivity, associated with obesity. Additionally, obesity is believed to be associated with an increased reactivity to adrenergic neurotransmitters, also leading to a reduction in blood flow to extremities [19-21].

A study done in females also showed that muscle sympathetic nerve activity is elevated in obesity resulting in increased muscle vascular resistance and levels of BP and decreased muscle blood flow. Increased insulin resistance/hyperinsulinaemia or baroreflex dysfunction may be the reason for this alteration [22].

The skeletal muscle is known to be the main target of action of insulin. Uptake of glucose in skeletal muscle is dependent on the effect of insulin on the skeletal muscle vasculature. It has been shown that the effect of insulin on skeletal muscle vasculature is to promote vasodilation, capillary recruitment and its own transendothelial transport by raised nitric oxide production through PI3K/Akt/eNOS pathway activation [23].

Resistance to insulin action is developed in obese by inability of insulin to inhibit glucose output from the liver and to promote glucose uptake in fat and muscle. There is an impairment of Nitric Oxide (NO) bioavailability resulting in impaired capillary recruitment in skeletal muscles due to insulin resistance in obesity. Previous studies have shown that with development of the obesity, there is a progressive microvascular rarefaction (a decrease in microvascular density) within multiple organs leading to decreased blood supply [24].

Renin-Angiotensin-Aldosterone System (RAAS) has a dual role, as it has both beneficial and deleterious effects in the skeletal muscle vasculature. In the vasculature, AT1R (angiotensin II receptor 1) activation increases oxidative stress and promotes vasoconstriction. In contrast, AT2R (angiotensin II receptor 2) activation produces vasodilation induced by the activation of the bradykinin/NO system. In obesity, there is an inappropriate activation of the RAAS with enhanced AT1R signaling causing vasoconstriction and thereby decreasing blood flow to skeletal muscles [23,25,26].

Increase in BMI is associated with stiffness of resistance arterioles and thickening of basement membranes and hence decrease in arterial lumen. This may be due to increase in the level of insulin (due to obesity induced insulin resistance) which has a direct trophic effect on vascular smooth muscle cells, by generation of reactive oxygen species, protein kinase C and by activation of NF-kB [19,27,28].

Moreover, in obesity, in order to acclimatise to raised pressure, the thickness of basement membrane of microvessels is increased and shunt system is used to redirect blood during meals or exercise. In severe obesity, atrophy begins in the walls of the microvessels, thus resulting in decrease in lumen, decreasing the ability to shunt, thereby increasing the risk of peripheral vascular disease [19,29].

The obese group had a blunted change in post-occlusive reactive hyperaemic blood flow, indicative of impaired vascular reactivity, than the normal weight group. Besides the negative consequences of obesity on vascular function in older populations, obesity-mediated alterations in endothelial function are evident even in young adults. A lower response in endothelial dependent vasodilation and forearm blood flow after an infusion of acetylcholine is observed in obese, young adults compared to overweight and normal weight young adults [8,30].

Atherosclerosis may also be a reason of decreased blood flow in obese as suggested by a study which showed association of childhood and adolescent obesity with an earlier appearance of these atherosclerotic lesions. Fatty streaks and fibrous plaques found in children who died from other causes were associated with previously measured BMIs [31].

LIMITATION

The present study was done only on young adult males. Further study involving a larger group of subjects including females should be done to extrapolate the results on a larger population.

CONCLUSION

We conclude that obese subjects though young had increased cardiac output and decreased peripheral blood flow as compared to subjects who were overweight and have normal BMI. If they continue to be obese, they may land up with cardiac complications like left ventricular hypertrophy, high output cardiac failure and peripheral artery disease in years to come. Since, these abnormalities are reversible at an early age, so to prevent the serious complications, weight should be controlled from young age. More and more emphasis should be given on healthy lifestyle from early age.

The NIVOMON series is a simple, novel, inexpensive and non invasive haemodynamic test that may replace other invasive haemodynamic test for screening vascular disorders in future at any age group.

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