

Association between Obesity and Peripheral Arterial Diseases among Non-smokers: A Cross-sectional Study

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ABSTRACT

Introduction: Obesity, especially abdominal obesity, is known to be a major risk factor for cardiovascular diseases. Peripheral Arterial Disease (PAD) is associated with obesity, and it is diagnosed using the Ankle-brachial Index (ABI). While the links between the ABI and cardiovascular diseases, such as myocardial infarction and stroke, are well established, its association with obesity has been studied less extensively.

Aim: The present study was undertaken to study the association between Body Mass Index (BMI), Waist-hip Ratio (WHR), Sagittal Abdominal Diameter (SAD) with ABI in Non-smokers and compare the results between obese and non-obese groups.

Materials and Methods: The present cross-sectional study was conducted from January to June 2018 with 160 non-smoking adults aged between 25 to 45 years, at the Lifestyle Laboratory in the Department of Physiology at Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India. The participants underwent a thorough assessment, during which their height, weight, Waist Circumference (WC), hip circumference, and SAD were measured. Body Mass

Index (BMI) and WHR were calculated for all individuals. The LifeDop 150R hand-held Doppler device and Diamond mercury sphygmomanometer were utilised to measure Ankle and Brachial Blood Pressure and to calculate the ABI. Statistical analyses included a t-test for comparing the two groups and a Chi-square test to examine the relationship between the two groups.

Results: In the present study, 160 non-smoking, non-diabetic, non-hypertensive adults aged between 25 to 45 years were examined, consisting of 132 females and 28 males. A significant association was found between the ABI and BMI when categorised as normal or abnormal BMI, but not when classified as normal, overweight, or obese. The obese and non-obese groups as per their WHR and SAD did not show a significant association with ABI.

Conclusion: In the present study, a significant association was found between obesity and PAD, as measured by BMI and ABI. Hence the relationship between obesity and changes in ABI values warrants extensive study.

Keywords: Ankle brachial index, Body mass index, Sagittal abdominal diameter, Vascular doppler, Waist-hip ratio

INTRODUCTION

One of the most common chronic metabolic diseases in the world is Obesity [1]. It is defined as excessive fat deposits that can impair health [1]. In 2022, a significant 43% of adults aged 18 and over were classified as overweight, while an alarming 16% were living with obesity [2]. Obesity leads to a continuous state of low-grade inflammation in the body, characterised by increased levels of inflammatory markers in the bloodstream [3-5]. It is widely recognised as a health hazard due to its link with various metabolic complications, including dyslipidemia, diabetes mellitus, hypertension, and cardiovascular incidents [6]. BMI is widely used to measure obesity because it is a simple calculation. However, BMI fails to provide information about the distribution of fat, and abdominal adiposity is a better predictor of cardiometabolic outcomes than BMI. Alternative measures of obesity include various parameters, such as WC, WHR, SAD, and Waist-to-height Ratio (WHR) [7].

Lower extremity PAD is defined as an ABI of less than 0.9 [8]. PAD increases the risk of cardiovascular disease and diminishes quality of life due to ischaemic leg pain and intermittent claudication [8,9]. While numerous studies [10-12] have explored the impact of obesity on cardiovascular health, few researchers have specifically examined its effects on the ABI [13]. The present study aimed to evaluate the impact of obesity on peripheral arterial vasculature in adults by using the ABI as the measurement tool. To ensure the exclusion of all confounding factors, the study included non-smokers, non-diabetics, and non-hypertensives as the subjects. The study considers three parameters of obesity: abdominal or

visceral obesity measured by the SAD and WHR, in addition to general obesity measured by BMI.

The study tested the null hypothesis that there will be no significant difference in ABI values between obese and non-obese individuals. The alternative hypothesis stated that individuals with obesity will exhibit significantly different ABI values compared to non-obese individuals. Hence the present study was conducted to establish an association of obesity parameters, such as BMI, WHR, and SAD, with the ABI.

MATERIALS AND METHODS

The present cross-sectional study was conducted from January to June 2018 at the Lifestyle Laboratory, Department of Physiology, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India. The study was commenced after receiving clearance from the Ethical Committee of Bangalore Medical College and Research Institute with the approval number {ACA/DCD/SYN/BMC-B/PG/2016-17}. The study follows the Helsinki Declaration of 1975, revised in 2013. All subjects were asked to visit the Lifestyle Laboratory in the morning. The procedure and objectives of the study were explained to each participant, after which written informed consent was obtained.

Inclusion criteria: The age group of 25 to 45 years is included as it represents a significant portion of the active workforce, allowing for potential correction of detected abnormalities through interventions. All the subjects included were non-smokers, non-diabetic and non-hypertensive based on the details given by them while taking the detailed history.

Exclusion criteria: Subjects with metabolic and endocrine disorders such as diabetes mellitus, thyroid disorders, Cushing's syndrome, growth hormone deficiency, hypertension, etc., Alcoholics, smokers and tobacco chewers, subjects with positive family history of PADs and other vascular disorders, and subjects taking drug therapies such as corticosteroids, contraceptives, beta-adrenergic blockers, etc., were excluded.

Sample size calculation: Sample size was estimated using the formula:

$$\text{Sample Size (n)} = \frac{(\text{Z}\alpha + \text{Z}(1-\beta))^2 \sigma^2}{d^2}$$

where, $\text{Z}\alpha$ =Alpha Error, $\text{Z}(1-\beta)$ =Beta Error, σ =Standard Deviation, d =Effect Size. Assuming power as 80% and alpha error of 5%, standard deviation (BMI), and effect size based on a previous study i.e., effect size= 3.39, $\text{Z}\alpha$: standard two-sided 5% critical value=1.96, $\text{Z}(1-\beta)$ =0.842, Standard deviation= 3.4 [14], the sample size calculated was 160, and the participants were recruited using simple random sampling.

Study Procedure

Data collection: To ensure accuracy, anthropometric parameters of participants were measured while wearing light clothing and after an overnight fast. Height, weight, WC, hip circumference, and SAD were measured. Each participant rested for at least 15 minutes before measuring ankle and brachial systolic blood pressures. A diamond mercury sphygmomanometer and a LifeDop 150R Doppler device were used for the measurements. The BMI was calculated as the ratio of body weight in kilograms and the square of height in meters, using Quetelet Index. Based on BMI, subjects were classified into three categories (both males and females): Normal- 18.0 to 22.9; Overweight - 23.0 to 24.9; Obese - 25.0 or greater [15].

The WHR was calculated for the subjects. Individuals were classified as non-obese if their WHR was below 0.88 for males and below 0.80 for females. Those with a WHR of 0.88 or higher for males and 0.80 or higher for females were classified as obese [15,16]. The SAD cut-offs are based on a study that found non-obese males had SAD measurements of less than 220 mm, and non-obese females had measurements of less than 200 mm. In the obese group, males had SAD of 220 mm or greater, while females had measurements of 200 mm or greater [17]. The ABI for the right leg was calculated using the formula: ABI=Highest ankle pressure (right leg)/Highest brachial pressure (both arms). An ABI of 0.9 or lower, or 1.4 or higher, significantly increases the risk of cardiovascular events and mortality. An ABI between 0.91 and 1.0 indicates borderline risk [8,18].

STATISTICAL ANALYSIS

The statistical software, namely SPSS 18.0, and the R environment ver.3.2.2 were used for the analysis of the data, and Microsoft Word and Excel were used to generate graphs, tables, etc., In this study, descriptive statistical analysis was conducted. Continuous measurements are presented as Mean \pm Standard Deviation (Min-Max). Statistical significance was evaluated at the 5% level. Analysis of variance (ANOVA) is used to assess the significance of study parameters among three or more groups of subjects. Meanwhile, the Chi-square test and Fisher's exact test are utilised to evaluate the significance of study parameters on a categorical scale between two or more groups.

RESULTS

The study involved 160 non-smoking, non-diabetic, non-hypertensive adults with a mean age of 35.28 ± 7.23 years. In present study, there were all non-smokers, including all women who had never smoked in their entire lives. Among the male participants, 10 were previously occasional smokers but had been abstinent for at least one year. Notably, these men had never smoked 100 or more cigarettes in their lifetime, which is the Centers for Disease Control and Prevention criterion for never-smoker [19].

[Table/Fig-1] shows the total number of subjects across the age groups. In the present study, majority 88 subjects were aged between 35-45 years. Study comprised 132 females and 28 males.

| Gender | Age in years | | Total |
|--------|--------------|------------|-------------|
| | 25-34 | 35-45 | |
| Female | 55 (76.4%) | 77 (87.5%) | 132 (82.5%) |
| Male | 17 (23.6%) | 11 (12.5%) | 28 (17.5%) |
| Total | 72 (100%) | 88 (100%) | 160 (100%) |

[Table/Fig-1]: Distribution of participants based on age and gender.

Pearson's Chi-square test.

In the present study, there was no significant difference in the distribution of subjects between the obese and non-obese groups. Furthermore, there was no significant difference among the three BMI categories: normal, overweight, and obese, nor between those with normal and abnormal BMI [Table/Fig-2].

| Variables | Gender | | Total (n=160) | p-value |
|-------------------------------|-------------------|----------------|------------------|---------|
| | Female (n=132) | Male (n=28) | | |
| BMI (kg/m²) | | | | |
| Normal | 68 (51.5%) | 10 (35.7%) | 78 (48.8%) | 0.223 |
| Over weight | 24 (18.2%) | 5 (17.9%) | 29 (18.1%) | |
| Obese | 40 (30.3%) | 13 (46.4%) | 53 (33.1%) | |
| BMI (kg/m²) | | | | |
| Normal BMI | 68 (51.5%) | 10 (35.7%) | 78 (48.8%) | 0.19 |
| Abnormal BMI | 64 (48.5%) | 18 (64.3%) | 82 (51.2%) | |
| WHR | | | | |
| Non-obese | 29 (22%) | 9 (32.1%) | 38 (23.8%) | 0.251 |
| Obese | 103 (78%) | 19 (67.9%) | 122 (76.3%) | |
| SAD (cm) | | | | |
| Non-obese | 86 (65.2%) | 21 (75%) | 107 (66.9%) | 0.315 |
| Obese | 46 (34.8%) | 7 (25%) | 53 (33.1%) | |

[Table/Fig-2]: Distribution of study population with respect to groups divided based on the obesity parameters and their gender.

Pearson's Chi-square test.

BMI, WHR, and SAD of participants were analysed for their association with ABI. The results showed no significant association between increasing BMI and ABI among the normal, overweight, and obese groups. However, a significant association was found when the groups were categorised as normal and abnormal BMI. Additionally, no significant associations were observed between ABI values and WHR or SAD when comparing obese and non-obese participants [Table/Fig-3].

| Variables | Ankle Brachial Index (ABI) | | | p-value |
|-------------------------------|----------------------------|--|-----------------|-------------------|
| | Normal | Overweight | Obese | |
| BMI (kg/m²) | 1.02 \pm 0.08 | 0.98 \pm 0.08 | 1.01 \pm 0.10 | 0.051 |
| | Normal | Abnormal (Overweight and Obese) | | |
| WHR | 1.02 \pm 0.08 | 0.99 \pm 0.06 | | 0.04 [*] |
| | Non-obese | Obese | | |
| SAD (cms) | 1.02 \pm 0.08 | 1.00 \pm 0.09 | | 0.198 |
| | Non-obese | Obese | | |

[Table/Fig-3]: Comparison of mean values of ABI according to the different anthropometric parameters used to group the subjects.

When three groups compared in BMI- One-way ANOVA test; 2 groups- Student's t-test WHR and SAD- 2 groups compared using Student's t-test.

DISCUSSION

In the present study, low ABI was significantly associated ($p<0.05$) with an increased BMI when compared amongst individuals with normal BMI to those with abnormal BMI thus rejecting the null

hypothesis. Notably, this relationship was observed regardless of the absence of hypertension, diabetes, cardiovascular issues, or other potential confounding factors.

While the BMI is commonly used, WC and WHR are more accurate predictors of Cardiovascular Disease (CVD) due to their association with visceral fat. The SAD is also considered a specific indicator of visceral obesity [15,20]; however, the present study hasn't included WC and has found no significant correlation between WHR or SAD measurements and the ABI.

Obesity leads to the release of substances that affect lipoproteins and inflammation, promoting atherosclerotic diseases. The reduction in blood pressure in the lower limbs may result from plaque formation in the arteries, leading to narrowed vessels and decreased blood flow. In a study conducted by Yeboah K et al., they found that obese Ghanaians ($BMI \geq 30 \text{ kg/m}^2$) with asymptomatic PAD had lower ABIs. Interestingly, among participants of different ethnicities, African-Americans had lower visceral fat levels despite similar BMIs and waist sizes compared to others [21]. Misra A et al., argue that using BMI as a universal cut-off for obesity is outdated [22], as body composition varies among individuals, which is supported by many other studies [23,24]. Asian Indians considered "non obese" had higher abdominal and visceral fat compared to Caucasians with similar BMIs [25]. Dyslipidaemia, characterised by high triglycerides and low High Density Lipoprotein (HDL) cholesterol, is more common in those with abdominal obesity, which is prevalent in Asian populations. Consequently, they face greater cardiovascular disease risk at lower BMIs [26,27]. Low Ankle Brachial Index (ABI) values are associated with cardiovascular diseases. A study by Leng GC et al., found that lower ABI values at baseline correlated with a higher risk of non-fatal myocardial infarction and stroke, as well as increased mortality from myocardial infarction and all cardiovascular causes. This suggests that low ABI is linked to a higher risk of non-fatal cardiovascular events and death, independent of age, sex, and baseline conditions like angina and diabetes [28].

According to the American Heart Association, individuals who show no symptoms, like the subjects in this study, can benefit from ABI testing. This test offers information beyond standard risk scores for predicting future cardiovascular events. Individuals with an ABI of 0.9 or lower, or 1.4 or higher, are at an increased risk of cardiovascular events and mortality, regardless of whether they experience symptoms of Peripheral Artery Disease (PAD) or possess other cardiovascular risk factors [29]. Further longitudinal studies are crucial, involving a larger and more diverse sample of subjects across various ages, socioeconomic backgrounds, and ethnic groups. It's also unclear which obesity parameters predict cardiovascular ill health. There is a need for research focused on the Indian population to incorporate ABI measurements into routine check-ups. This integration could facilitate the early identification of individuals at risk for peripheral artery disease PAD or CVD.

Limitation(s)

The study categorised groups into obese and non-obese based on three anthropometric parameters, resulting in an unequal distribution that may have affected the results, despite appropriate matching. Additionally, the sample included more women than men, which may have introduced bias. The findings are mainly relevant to the South Indian population, limiting their generalisability to other ethnic groups. Lastly, as the study utilised a cross-sectional design with measurements taken only once, it creates uncertainty regarding the temporal relationships between exposure and outcomes, despite previous studies linking central obesity to increased cardiovascular disease risk.

CONCLUSION(S)

Individuals with abnormal BMI had significantly lower ABI values than those with normal BMI, indicating the impact of obesity on

peripheral arterial vasculature. Other obesity measurements, like WHR and SAD, did not show a relationship with peripheral arterial health, underscoring the relevance of BMI for assessing obesity in Indians. The relationship between obesity and changes in ABI values warrants extensive study, as it may help in diagnosing or predicting cardiovascular disorders in individuals.

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