A Comparative Study of Autonomic Cardiovascular Parameters in Obese and Non-Obese Adults.

Hari Mohan Prasad Sinha[1], Bipin Bihari Pradhan[2], Arsalan Moinuddin[1], Ashish Goel[3], Rajesh Misra[4], Priyanka Gupta[1], Arunima Deep[5], Devina Aswal[6]

[1]Assistant Professor, Department of Physiology, Shridev Suman Subharti Medical College, Dehradun, Uttarakhand.
[2]Professor, Department of Physiology, SCB Medical College, Cuttack, Orissa.
[3]Associate Professor, Department of Physiology, Shridev Suman Subharti Medical College, Dehradun, Uttarakhand.
[4]Professor, Department of Physiology, Shridev Suman Subharti Medical College, Dehradun, Uttarakhand.
[5]Senior Resident, Department of Physiology, Shridev Suman Subharti Medical College, Dehradun, Uttarakhand.
[6]Junior Resident, Department of Physiology, Shridev Suman Subharti Medical College, Dehradun, Uttarakhand.

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ABSTRACT

Background: Globally, the epidemic of obesity in children and young adults is on a constant rise over the past decade. Obesity makes individual highly susceptible to a variety of chronic diseases and their complications. An altered autonomic response in the form of enhanced baseline sympathetic activity, feeble response to sympathetic stimuli and compromised parasympathetic activity is observed in obesity. We have assessed potentially perturbed autonomic responses in young overweight/obese first year medical students. **Methods:** This cross sectional analytical study was undertaken in the research lab of the Department of Physiology, M.K.C.G. Medical College over a period of 12 months on 300 students (both males and females) to determine sympathetic and parasympathetic responses to stress using hand-grip dynamometer and sinus arrhythmia test respectively. Independent 't' test, Pearson's correlation coefficient and multiple linear regression analysis in SPSS 20.0 was used to statistically ascertain the differences for the aforementioned parameters between obese and non-obese adults. **Results:** Weight, Body mass index (BMI), waist hip ratio (WHR), Pulse rate (PR), baseline systolic blood pressure (BSBP) & baseline diastolic blood pressure (BDBP) is significantly greater in obese than in non-obese. BMI shows positive correlation with BSBP & BDBP (r=0.660**; p<0.001 & 640**; p<0.001) and negative correlation with ΔDBP, and E/I Ratio. A negative correlation is appreciated amongst ΔDBP and BMI (R^2 = 39.6). A similar negative correlation is again seen between E/I ratio and BMI (R^2 = 37.2). **Conclusion:** Obesity potentially alters autonomic balance with increased sympathetic and reduced parasympathetic tone posing elevated risk of cardiovascular and cerebrovascular accidents.

Keywords: Body mass Index, Handgrip test, Sinus arrhythmia test.

INTRODUCTION

Globally, the epidemic of obesity in children and young adults is on a constant rise over the past decade. Its prevalence in India ranges from 10% to 40% and it is more likely to increase with age at least up to 50 years.[1] Classically obesity is characterized by increased body fat (BF), associated with dyslipidemia, insulin resistance, cell organelles stress, and vascular inflammation. Increased weight makes obese individual highly susceptible to cardiovascular, cerebrovascular, respiratory, pulmonary, and renal ailments along with obstructive sleep apnea and different types of malignancies.[1,2]

Name & Address of Corresponding Author
Dr. Hari Mohan Prasad Sinha
Assistant Professor,
Department of Physiology,
ShridevSumanSubharti Medical College,
Dehradun, Uttarakhand

In general obesity results from greater energy intake than expenditure. Once greater amount of energy from food enters the body than needed it increases the body weight. This excess energy is stored as fat in adipocytes causing obesity. The etiology of obesity is multifactorial. To some extent genes determine food intake and energy metabolism along with various lifestyle and environmental factors.[2] The rapid rise in obesity off late vehemently suggests the key role of lifestyle and environmental factors because genetic changes alone could not have occurred so rapidly.[2]
Most noticeably, obesity has been added recently as an independent risk factor in the etiology of hypertension.[16] The American Heart Association (AHA) has reported greater prevalence of hypertension amongst obese individuals.[15,16] Chronically augmented sympathetic and attenuated parasympathetic activity perhaps forms the ramification mechanisms underlying the pathophysiology of hypertension in obese

population. An overall perturbed autonomic response which includes chronically enhanced baseline sympathetic activity, feeble response to sympathetic stimuli and compromised parasympathetic activity is observed in both overweight/obese.[3,4]

To the best of our knowledge most of the available data suggesting autonomic variations in overweight/obese individuals focuses on age-groups in excess of 30 years of age. However, the exiguity of available researches on the autonomic dysfunction amongst young overweight/obese adults (18-25 years) compel us to take the present study with an aim to investigate the changes in sympathetic & parasympathetic autonomic parameters amongst young obese medical students of M.K.C.G. Medical College, Berhampur, Orissa.

MATERIALS AND METHODS

Study design

This cross sectional analytical study was undertaken to investigate the changes in sympathetic and parasympathetic autonomic parameters in young obese students of M.K.C.G. Medical College, Berhampur, Orissa. The research was carried out in the research lab of the Department of Physiology, M.K.C.G. Medical College after obtaining written consent from all participants.

Sample population

Volunteers (18-25 years) were selected from a representative group of students MBBS 1st year students (both male and female) of MKCG Medical College. They were divided into two groups based on the WHO classification of obesity.[18] Inclusion criteria for Control were clinically healthy volunteers with BMI < 25 kg/m2 and for overweight/obese was BMI > 25 kg/m2. Exclusion criteria comprised of history of diabetes mellitus, diagnosed CVD, smokers, alcoholics, obesity, disabled, past/concurrent pulmonary illness, Reynolds phenomenon, symptoms of atopy/allergy.

Sample size

A sample size of 150 for each group was calculated through Cohen flexible algorithm using Fischer's 'F' as a basis to calculate sample size to compare means between groups.[11] This algorithm produces sample size for two or more than two groups using distributions to calculate sample size inevitably minimizing incurring rounding errors, thus augmenting the results from calculations. In our case, keeping 'α'=0.05, 'β'= 80%, using Fischer's tables 'F'= 0.7 / 2 * 1 = 0.35 and effect size (es) (difference between the two groups / 2 * within the group SD; which is equal to 0.7)

Baseline anthropometric measurements

All the tests were performed between 9.00 A.M. to 11.00 A.M. on the study days to avoid variation due to circadian rhythm. The subjects had light breakfast without tea or coffee. Weight was recorded using "Krups" weighing machine to the least of 100 grams (gm). Height was measured as standing height by measuring tape in cms to the nearest of 1 cm. BMI was subsequently calculated from the abovementioned parameters. Waist Circumference (WC) was measured at the level of umbilicus without compression of skin whilst hip circumference (HC) was measured across greater trochanter. Waist-hip ratio (WHR) is then calculated as the ratio of WC and HC and is the measure of central pattern of fat distribution. The room temperature was maintained at 25° C using air-conditioner. Pulse rate, blood pressure and oxygen saturation were measured by Cardiac Monitor.

Cardiac monitoring

Cardiac monitoring was done using ClarityMed PMS 320 to measure the blood pressure, heart rate, and oxygen saturation of the subjects. PMS 320 combines a powerful hardware platform with software employing advanced digital signal processing to give accurate readings. Its compact size and portability makes the instrument ideal for both continuous and real time recording. Pulse Oximetry works by applying a sensor to a pulsating arteriolar vascular bed. The censor contains a dual light source on one side and photo-detector on the other side. Bone, tissue, pigmentation, and venous vessels normally absorb a constant amount of light over time. The arterial blood amount varies during systole and diastole thereby resulting in absorbing variable amount of light. The ratio of light absorbed at systole and diastole is translated into an oxygen saturation measurement. The subject was connected to the monitor i.e. the blood pressure cuff is tied around the non-dominant arm, and the censor is attached to the index finger of the non-dominant hand of the subject. Oxygen saturation (SpO2) and heart rate was continuously displayed on the monitor. For measuring the blood pressure, the BP button on the control panel was pressed and the blood pressure was recorded and displayed on the screen. The accuracy of heart rate measured was ±3 beats per minutes, while that of SpO2 is ±2 digits (range 70-100%) and ±3 digits (range of 50-60%). The accuracy of blood pressure recorded was ±5mm of Hg.

Hand Grip Dynamometer

The Handgrip Dynamometer (HGD) is a hand held device capable of measuring instantaneous hand strength as a function of time. It is routinely used to assess the sympathetic response in the body. In our study, MED SCALE Dynamometer is used. It is a spring loaded resistance dynamometer which can measure the maximum isometric strength of the hand and forearm muscles. Initially, baseline BP was recorded in sitting position. The subjects were asked to grip the Handgrip Dynamometer as much as they can with their dominant hand. This was repeated 3 times and the average of three consecutive maximum attempts were calculated. This gave the Maximum Voluntary Contraction. Then the subject was asked to hold the dynamometer in the dominant hand, the handle of the dynamometer rest on first metacarpal (heel of palm), while the handle should rest on middle of four fingers. With the arm at right angles and the elbow by the side of the body, the subject then squeezes the dynamometer and maintains the pressure on dynamometer at 30% of the Maximum Voluntary Contraction. No other body movement is allowed. The blood pressure and heart rate were recorded at 1st minute and 2nd minute of contraction. The alteration in the blood pressure and heart rate just before the release of hand grip test was taken as the index of response to hand - grip test. To summarize, resting systolic and diastolic BP (mmHg), resting HR (beats/min), systolic and diastolic BP (mmHg) just before release were measured throughout. Difference in diastolic BP (ΔDBP) just before release was used for analysis (17). The accuracy of the instrument was ±3 pounds

Expiration/Inspiration (E/I) Ratio measurement

E/I ratio was measured to assess and reinforce parasympathetic modulation. Respiratory excursions were obtained using stretch sensitive strain gauze with Velcro straps tethered around the chest and connected to the polygraph machine. The subject took slow deep inspiration for 5 seconds followed by slow deep expiration for another 5 seconds thus making each respiratory cycle last for 10 second. This was ensured by entraining the subject repeatedly well in advance before the experiment using a stop watch. Six such cycles were recorded each minute for 5 minutes with the simultaneous recording of ECG. Finally, ratio of the longest R-R interval during expiration to the shortest R-R interval during inspiration (E/I ratio) was calculated from above obtained respiratory and ECG tracings.

Statistical Analysis

Dataset was analyzed using SPSS (Statistical Package for the Social Sciences; version 20.0 for Windows). Independent‘t’ test was used for comparing continuous variables (anthropometric indices and cardiovascular parameters) between the groups. Pearson correlation co-efficient was used to find mutual correlation between age, weight, BMI (body mass index), BSBP (baseline systolic blood pressure), BDBP (baseline diastolic blood pressure), Difference in diastolic blood pressure (ΔDBP), Expiration/Inspiration (E/I) Ratio in overweight/obese subjects (n=150). The above mentioned parameters were further evaluated using linear regression analysis to decipher interrelationship between dependent variables of ΔDBP and E/I ratio with BMI as independent variable.

RESULTS

A dataset of 300 students from MKCG Medical College were analysed; (men: 62%, mean age: 19.5 years, & S.D: ±1.12, women: 38%, mean age: 19.3 years, SD: ±1.02) Overall men have higher frequency of stroke hospitalization and higher mean age than men.

[Table 1] shows that overweight/obese individuals were slightly older but this difference for age was statistically non-significant ($p > 0.05$) thus maintaining homogeneity amongst the two groups. The demographic and clinical parameters of BMI, WHR, resting heart rate, baseline systolic blood pressure and baseline diastolic blood pressure in overweight/obese individuals was accentuated as compared to the control group and this difference between the two groups is statistically significant (p,0.05). This difference is least appreciated in WHR but it is still statistically significant.

[Table 2] shows correlations of age, weight, BMI, WHR, BSBP, BDBP ΔDBP, and E/I Ratio each other among overweight/obese subjects. BMI showed positive correlation with BSBP & BDBP (r=0.660**; p<0.001 & 640**; p<0.001) and negative correlation with ΔDBP, and E/I Ratio (r = -0.628**; p<0.001 r = -0.602**; p<0.001). The parameters of ΔDBP and E/I ratio showed negative correlation with all the comparable variables except age.

Table 1: Comparison of baseline anthropometric and clinical parameters between overweight/obese and normal subjects.

Parameter	CONTROL (n=150) M ± SD	OVERWEIGHT/OBESE (n=150) M ± SD	‘P’ value
Age (years)	19.40 ± 1.08	19.46 ± 1.10	P>0.05
Weight (Kilograms)	63.18 ± 7.14	78.91 ± 5.50	P<0.05
BMI (Kg/m2)	21.38 ± 2.23	29.89 ± 2.90	P<0.05
Waist Hip Ratio	0.90 ± 0.06	0.98 ± 0.44	P<0.05
Pulse Rate (beats/min)	74.93 ± 7.10	86.16 ± 10.63	P<0.05
Baseline Systolic Blood Pressure (mmHg)	113.20 ± 7.26	148.04 ± 8.19	P<0.05
Baseline diastolic Blood Pressure (mmHg)	74.44 ± 5.12	92.04 ± 4.16	P<0.05

Data was presented as mean ± standard deviation. Analysis was done using ‘Independent‘t’ test’ P<0.05.

Table 2: Pearson correlation of age, weight, BMI, BSBP, BDBP, ΔDBP, E/I ratio with each other in overweight/obese subjects (n=150).

Parameters	Age (Years)	Weight (Kg)	BMI (Kg/m2)	BSBP (mmHg)	BDBP (mmHg)	ΔDBP (mmHg)	E/I ratio
Age (Years)	1	r = 0.103	r = 0.049	r = 0.011	r = 0.039	r = 0.052	r = 0.002
Weight (Kg)		1	r = 0.704**	r = 0.508**	r = 0.497**	r = -0.436**	r = -0.440**
BMI (Kg/m2)			1	r = 0.660**	r = 0.640**	r = -0.628**	r = -0.602**
BSBP (mmHg)				1	r = 0.779**	r = -0.796**	r = -0.582**
BDBP (mmHg)					1	r = -0.745**	r = -0.473**
ΔDBP (mmHg)						1	r = 0.561

r = Pearson's correlation coefficient, *P<0.01; **P<0.001; BMI (Body mass index), BSBP (Baseline systolic blood pressure), BDBP (Baseline diastolic blood pressure), ΔDBP (Difference in diastolic blood pressure), E/I ratio (Expiration /Inspiration ratio)

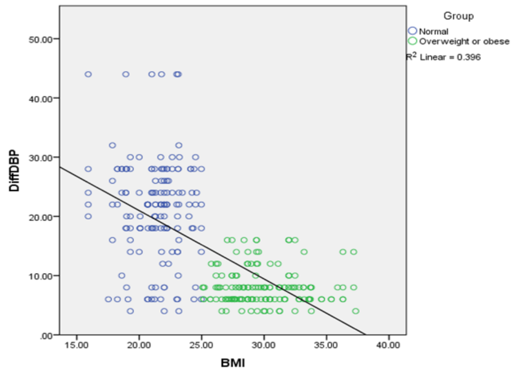

Figure 1: Simple linear regression analysis for BMI & ΔDBP (diffDBP)

[Figure 1] compares dependency of ΔDBP on BMI between overweight/obese and controls using simple linear regression analysis. A negative correlation is appreciated amongst ΔDBP and BMI and around 39.6% of attenuated ΔDBP is explained by increasing BMI (R2 = 39.6). Thus, an increase in BMI (in overweight/obese group) narrows down the difference between baseline DBP and DBP at the time of maximum contraction (ΔDBP). This can be partly due to high baseline DBP at rest and due to compromised rise in DBP during height of contraction as a result of blunted sympathetic response.

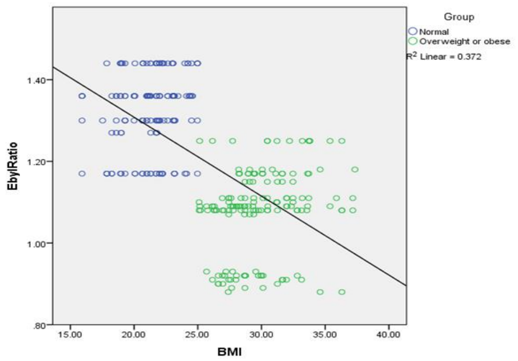

Figure 2: Simple linear regression analysis for BMI & E/I ratio (EbyIratio)

[Figure 2] compares dependency of E/I ratio on BMI between overweight/obese and controls using simple linear regression analysis. A similar negative correlation is again seen between E/I ratio and BMI and around 37.2% of lowering of E/I ratio is explained by increasing BMI (R2 = 37.2).

DISCUSSION

Obesity has been added as an independent risk factor in the etiology of hypertension. It was thought to be associated with altered autonomic activity i.e. increased sympathetic and reduced parasympathetic activity for a while. The on-board MONA LISA hypothesis (Most Obesities kNown Are Low In Sympathetic Activity) states that obese individuals have reduced sympathetic activity which lowers thermogenesis in them causing positive energy balance and obesity.[5-7] Our study found a potential positive correlation between obesity and blunted sympathetic activity i.e. the sympathetic response to stress as shown by Hand grip dynamometer test was found diminished in overweight/obese individuals with an increase in BMI. Autonomic function tests such as sustained hand-grip dynamometer test have been widely used to assess sympathetic activity. It involves exercising muscle along with central command which traverses to the muscle and heart raising systolic BP, diastolic BP and HR with an appreciable effort and time-dependent increase in muscle sympathetic activity. This rise in BP is mediated by an in¬crease in cardiac output and peripheral resistance whereas the early HR increase seems to be due to vagal withdrawal. The results (rise in SBP, DBP, and HR) during the latter half of the test while approaching towards the end when the subject cannot sustain handgrip anymore were elicited by sympathetic activation. This hand grip strength probably decreases in obese individuals when subjected to isometric exercise.[8,9]

We found a diminished gap in ΔDBP amongst overweight/obese individuals as compared to controls which exhibits an altered sympathovagal balance. This can be partly due to high baseline DBP at rest and also due to compromised rise in DBP during height of contraction as a result of blunted autonomic response.[12] Victor RG et al. stated that hand grip dynamometer test is an isometric exercise producing significant increase in BP due to increased sympathetic activity mediated by α - adrenergic receptors of autonomic nervous system.[10] An increase in sympathetic activity in response to handgrip test is a result of impulses from limbic cortex and proprioceptors in the small hand joints acting as afferent inputs into the medullary cardiac centers causing increase in blood pressure both SBP and DBP.[10] The results showed that sustained isometric exercise results in significant decrease in both SBP and DBP. It is hypothesized that higher baseline blood pressure in overweight/obese group is due to higher vasoconstrictor tone and increase in cardiac output is due to increased circulatory overload on heart as a conspicuous consequence of increase in body mass index. The lower blood pressure response to hand grip test in obese group is more likely be due to either a lower sympathetic activity or lower peripheral vascular resistance in response to normal or subnormal para-sympathetic stimulation.[8]

Our results assessing parasympathetic efferent to heart using deep breathing test (sinus arrhythmia) showed a statistically significant decline in E//I ratio in overweight/obese individuals when compared with controls. This is in accordance with an epidemiological study by Wu J S et al who found a significant reduced E/I ratio among overweight/obese individuals.[13] Similar results of significant diminution of E/I ratio among prehypertensive off-springs of hypertensive parents was shown in a study by G K Pal et al.[12] It is known that reduced E/I ratio signifies impaired cardiac vagal tone which exists prior to the onset of overt hypertension. Sinus arrhythmia mainly results from spillover of signals from the medullary respiratory centre into the adjacent vasomotor centre causing alternate increase and decrease in the heart rate during inspiratory and expiratory cycles of respiration.[14] A decline in parasympathetic vagal activity among overweight/obese individuals increases heart rate during expiration which reduces E/I ratio.

CONCLUSION

As a whole, obesity potentially alters autonomic balance with increased sympathetic and reduced parasympathetic tone posing elevated risk of cardiovascular and cerebrovascular accidents. A further conscientious effort is required to elaborate this hypothesis more thoroughly on a larger cohort across a myriad of populations.

Limitations of the study

We have to rely on the accuracy and authenticity of the information provided by the students and also on the tools available to access the above mentioned data. We cannot rule out the possibility of publication bias in our literature search because most of the journal articles tried to correlate BMI and compromised sympathetic response to stress in some way or the other despite inconsistency in their results.

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