

www.ijabpt.com

Received: 24th June-2015

Volume-6, Issue-3, July-Sept-2015 **Coden IJABFP-CAS-USA** Revised: 3rd July -2015

ISSN: 0976-4550

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ASSESSMENT OF CARDIOVASCULAR AUTONOMIC FUNCTION IN ASYMPTOMATIC **OBESE YOUNG ADULTS – PREVENTION IS BETTER THAN CURE**

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ABSTRACT

Back ground: Obesity is emerging global epidemic in young adults who form the productive group of the society. This has been called as new world syndrome and is a massive reflection of social, economic and cultural problems currently faced by the developing and developed countries. As cardiac autonomic dysfunction often coexists with obesity, early detection of autonomic impairment by simple investigations of autonomic function, can be potentially important to prevent future complications.

Objective: To identify cardiovascular autonomic dysfunction in asymptomatic obese young adults.

Study design: This study was conducted in the department of Physiology at Kakatiya Medical College, Warangal, A.P. 30 apparently healthy obese subjects of both sex with BMI > 25 kg/sqm were taken as study group. Age and sex matched 30 normal weight subjects (BMI 18.5-22.9 kg/ sqm) taken as control group.

Methods: Ewing's battery of 5 noninvasive cardiovascular reflex tests were done for assessing autonomic function. These autonomic function parameters were correlated with BMI, Unpaired Student't' test and Pearson correlation coefficient test were used for statistical analysis.

Results: Mean values of all cardiovascular reflex tests were significantly lower in the study group.

Conclusion: The results indicate that cardiovascular autonomic dysfunction is present in otherwise healthy obese young adults.

Key words: Obesity, Autonomic function tests, cardiovascular autonomic dysfunction, body mass index.

INTRODUCTION

The global epidemic of overweight and obesity termed "globesity" is the major public health problem in developed as well as developing world. Rates of obesity have tripled over the last 20 years, where the prevalence of obesity ranges from 2%-10% world-wide (Hossain. P et.al 2007). Prevalence of overweight and obesity problem is much higher in urban population (Nishter, S 2007).

According to National Family Health Survey data, 12.1% males and 16% females of Indian population are obese/ overweight and Andhra Pradesh with 17.6 % males, 22.7 % females. Almost 65% of urban Indians are either overweight or obese (NFHS India national report 2006). Obesity is the fifth leading risk factors for global deaths, leading to 2.8 million deaths each year as a result of being obese.

Obesity is defined as abnormal or excessive fat accumulation that may impair health. An imbalance between calories consumed and calories expended is the fundamental cause of obesity and overweight. The National Institutes of Health and WHO recently adopted similar body weight guide-lines for over-weight and obesity (DHHS 1998) (WHO Report 1998) with world-wide increasing rates of obesity steadily. Body Mass Index -BMI, values of body weight adjusted for height provides most useful population level measure of over-weight and obesity as it is the same for both sexes and for all ages of adults. BMI = Weight in Kilograms / (Height in meters)². BMI 23 to 24.9 is considered as overweight and BMI \geq 25, as obesity for Asians, which are lower than the WHO standards where overweight and obesity are indicated by BMI \geq 25 and \geq 30 respectively (Weisell RC. 2002).

Vijetha et al

Raised BMI is a major risk factor for non communicable diseases such as cardiovascular diseases like hypertension and stroke which was the leading cause of death in 2008 (WHO Tech Pep 2000). Overweight adolescents are more likely to have hypertension in adulthood (Bao W et.al 1995) than lean individuals. Prevalence of essential hypertension in individuals with excessive stored fat is much higher than in individuals with normal habitués.

Increased sympathetic nervous system i.e., SNS activity is a critical connection between visceral adiposity and high blood pressure (Davy et.al 2009). SNS is the main regulatory mechanism of cardiovascular system and it is a strong candidate to explain this association. At an early stage autonomic dysfunction may be asymptomatic or mildly symptomatic. Early diagnosis is essential for maximum benefit (Gosh. Asuthosh et.al 1998) as autonomic neuropathy carries worst prognosis. Obesity is associated with ANS dysfunction which may cause various cardiovascular and metabolic complications.

Awareness of weight status is an important determinant in weight loss attempts. Weight loss has shown to decrease these health risks associated with obesity. Beneficial effects were observed on hypertension and diabetes mellitus (Elmer PJ et.al 2006) with modest amount of weight loss.

The present study is done to assess relationship between ANS and obesity using autonomic function tests as diagnostic tool, so that early detection of autonomic dysfunction would help to warn about the risks of landing up with cardiovascular abnormalities and also to enlighten the benefits of weight reduction for a happier life, in view of the rising trends of overweight and obesity.

MATERIALS AND METHODS

This study was done in the department of Physiology of Kakatiya Medical College, Warangal. For this study 60 healthy subjects of 18-30 years of age of both sex were selected from different areas Warangal city. The purpose and expected outcome of the study were explained to each subject and encouraged for voluntary participation and informed consent was taken from each subject. Ethical committee approval was obtained. Detailed medical and family history was taken and thorough clinical examination was done. All information was recorded in a preformed questionnaire. Height and weight of the subjects were recorded and BMI was calculated. Then the cardiovascular reflex tests were determined by using physiograph the lab tutor. Each of the subjects was briefly explained about the procedure in detail and encouraged to obtain maximum efficient performance. Autonomic function tests were conducted in a comfortable environment in the departmental physiology laboratory from 9.00am - 2.30pm. By using unpaired student't' test with the help of Graph Pad calculator software the results were analyzed.

SELECTION OF SUBJECTS

Inclusion criteria: 18-30 years of age group of both sex, healthy individuals

Exclusion criteria: cardiovascular diseases, chronic obstructive lung diseases, smoking, hypertension, chronic renal failure or mental disorders which could alter the ANS function.

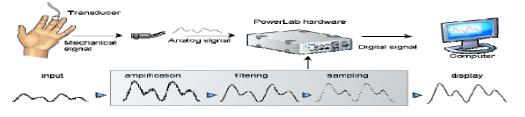
Control group:30 subjects with BMI <22.9 kg/m².</th>Study group:30 subjects with BMI \geq 25 kg/m².

Study design: Comparative study

METHOD

Quantitative autonomic function tests by Ewing and Clark, non-invasive cardiovascular reflex tests were done using digital physiograph, the lab tutor. Lab Tutor designed specifically for teaching in labs is based on HTML-software package, and used in conjunction with AD Instruments' Power Lab. The lab tutor does sampling, digitizing and storage of experimental data, display, and analysis of data which has a display panel showing a section of a conceptual strip of electronic data chart.

Data Acquisition: The signal of interest is converted into an analog voltage, amplitude of which usually varies over time, and is monitored by the recording hardware, which can modify the signal by filtering and amplification i.e., 'signal conditioning'. The resulting signal is sampled at regular intervals and converted from analog to digital form and transmitted to the computer, where the sampled data is stored and displayed.



Autonomic Function Tests: These are simple non-invasive cardiovascular reflex tests, easy to use and provide quantitative information about autonomic function.

- 1. Heart rate response to standing
- 2. Heart rate response to deep breathing
- 3. Heart rate response to Valsalva maneuver
- 4. Blood pressure response to standing
- 5. Blood pressure response to sustained hand grip

Tests to determine Parasympathetic activity:

i) **HR response to standing:** The ECG limb leads were attached to the subject and connected to the lab tutor, the subject was asked to stand from lying as quickly as possible with strip recorder running (II), and 30:15 ratio is measured.

30:15 ratio: Ratio of longest R-R interval around 30th beat after standing to shortest R-R interval about 15 beats after standing.

30:15 Ratio- Normal <a>> 1.04, Borderline 1.01-1.04, Abnormal <a> 1.00

ii) HR response to deep breathing.

With the subject sitting and strip ECG recording, the subject was asked to breathe deeply and evenly at 6 breaths per minute (5 seconds in; 5 seconds out) for 3 cycles in 30 seconds and count "IN-2-3-4-5-OUT-2-3-4-5-as they do.

E/I ratio – Ratio of maximum to minimum R-R interval during expiration and inspiration respectively. E/I ratio - Normal: \geq 1.21, Abnormal: \leq 1.20

iii) HR response to Valsalva manoeuvre.

The subject was asked to blow into a mouthpiece attached to a sphygmomanometer against 40mmHg for 15s; the system should have a slow leak to ensure that the subject strains continuously and not falsely maintain pressure by glottis closure of the airway. Record for 30 seconds more after this manoeuvre with patient sitting and strip ECG recording. Repeat twice, and average the ratio from the 3 Valsalva attempts was taken to calculate valsalva ratio.

Valsalva ratio: ratio of longest R-R interval within 20 beats of ending manouvre to shortest interval during manoeuvre. **Normal:** \geq **1.21, Abnormal:** \leq **1.20**

Tests to determine sympathetic activity:

iv)BP response to standing

The subject was made comfortable and asked to lie down on the couch and relax; initial BP was recorded on the digital physiograph. The subject was asked to stand up immediately and BP was recorded after 1minute. Difference in systolic blood pressures between lying and after standing for 1 minute is calculated.

Normal: <10 mmHg, Borderline: 11-20 mmHg, Abnormal: <a>>30 mmHg

v) BP response to sustained handgrip.

The subject's resting blood pressure was recorded. Then asked to maintain handgrip in other arm at 30% of maximum voluntary pressure (use dynamometer) for up to 5 minutes; and BP was recorded each minute up to 4minutes. Difference in the diastolic BP before and after sustained handgrip is calculated.

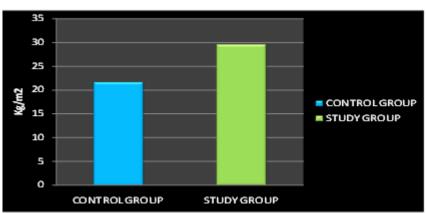
Normal: >16 mmHg, Borderline: 11-15 mmHg, Abnormal: <10 mmHg

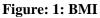
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RESULTS

Comparison of BMI between the study group and the control group which is statistically significant is shown in the table: 1 and represented graphically in figure 1. Between group comparison of the 30:15 ratio, E/I ratio, Valsalva ratio are depicted in Table: 2, Table-3, Table-4, table-5 respectively which showed that means of study group are significantly lower than that of the control group and are represented graphically in figure 2, 3,4 respectively. Between group comparisons of BP response to standing, BP response to sustained handgrip are depicted in Table-6 and Table-7 respectively with graphical representation in figure 5 &6 respectively.

BMI	Control Group	Study Group
Mean±SD	21.641±1.521	29.603±4.283
t Value	9.595	
p Value	0.0001	
Significance	Extremely Significant	







e-2: Detween (Foup Comparison	DIIS OF 30:15	rauo (H)	R Response to Stan
30:15 Ratio	Contr	Control Group		Study Group
MEAN±SD	1.33±(1.33±0.279		1.082±0.119
t Value		2.8979		
p Value		<0.0001		
Significance		Significant		
1.4 1.2 1 0LF 0.8 50 0.6 0.4 0.2 0				CONTROL GROUP
	ONTROL GROUP	STUDY GRC	UP	



E/I Ratio	Control Group	Study Group
MEAN±SD	1.22±0.085	1.067±0.198
t Value	3.8892	
p Value	0.0003	
Significance	Extremely significan	nt

Table-3: Between Group Comparisons of E/I Ratio -HR Response to Deep Breathing

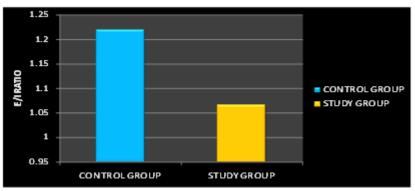


Figure 3: HR Response to Deep Breathing

Table-4: Between Group Comparison of HR Response to Valsalva Ratio

Valsalva Ratio	Control Group	Study Group	
MEAN±SD	1.453±0.236	1.193±0.235	
t Value	4.2759		
p Value	0.0001		
Significance	Extremely significant		

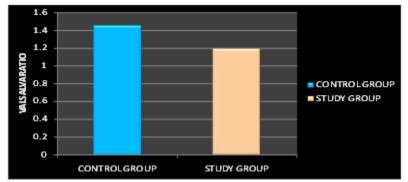


Figure 4: HR Response to Valsalva

Table-5: Between	Group C	Comparison	of BP Resi	oonse to Standing
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SBP Supine – SBP Standing	Study Group	Control Group
Mean±SD	8.933±4.249	11±10.272
t Value		1.015
p Value	0.3127	
Significance	Not significant	

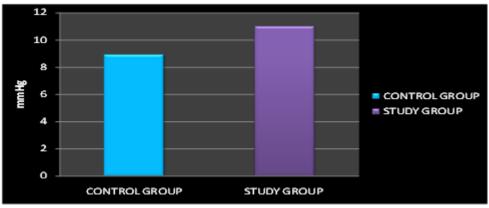


Figure 5: BP Response to Standing

Table: 6-Between Group Comparisons of BP Response to Sustained Handgrip

DBP During Sustained Handgrip – DBP AT Rest	Study Group	Control Group
MEAN±SD	15.8±6.204	10.933±6.526
t Value	2.8979	
p Value	0.0053	
Significance	Significant	

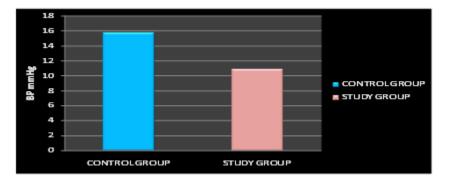


Figure 6: BP Response to Sustained Hand Grip test

DISCUSSION

The present study revealed, Heart rate response to standing (30:15 ratio), Heart rate variation during deep breathing (E/I ratio), Heart rate response to the Valsalva maneuver (valsalva ratio) in overweight and obese young adults is significantly lower when compared to that control group and Blood Pressure response to sustained handgrip is significantly less in obese when compared to control group.

These results point to the presence of cardiac vagal dysfunction and decrease in sympathetic function which suggest impairment of autonomic function in otherwise healthy obese young adults.

Sympathetic activity decrease may be the primary reason for excessive energy storage, or it may be the reflection of any other unknown factor or factors. Multiple factors like increased levels of leptin, insulin, non essential fatty acids, and angiotensin-II, reduced circulating concentrations of adiponectin or ghrelin play role in sympathetic nervous system activity. Body weight and the level of stored calories remain constant over long periods of time, suggesting that integrative control mechanisms couple energy expenditure and food intake. A regulatory system that maintains constant energy storage is likely to involve complex interactions among humoral, neural, metabolic, and psychological factors, and it has been suggested that the ANS may be central in the coordination of this system (Bray GA et.al 1979). Some researchers suggested that gradual development of insulin resistance in target tissues with the beginning of excess weight gain in obesity is responsible for subsequent development of hyper-insulinaemia (Steering Committee. The Asia-Pacific Perspective, 2000).

Vijetha et al

This hyperinsulinaemia has got a role in low cardiac vagal activity in obese person (Rissanen P et.al 2011)Our results are consistent with the study of "Relationship Between Obesity And Parasympathetic Nerve Function" done by Shahin Akhter, Noorzahan Begum, Sultana Ferdousi, Shelina Begum, Taskina Ali (Shahin Akhter et.al 2008).

"Cardio-respiratory interaction and autonomic dysfunction in obesity", study done by (Tonhajzerova et.al, 2008) showed that theDeep Breathing test was marginally significantly lower in the obese group compared with controls (Tonhajzerova et.al 2008) which is in correlation with our study.

Our study observations are similar with the study "Autonomic Neuropathy in Obesity" done by Shahin Akhter (Shahin Akhter et.al 2011)

Simran Grewal, Vidushi Gupta in their study "Effect of Obesity on Autonomic Nervous System" (G Simran et.al 2011) results indicates impaired vagal function in obese, which is similar to our study. Our findings are also in correlation with the study "Haemodynamic response to an isometric exercise test in obese patients: Influence of autonomic dysfunction" done by Valensi P et., al. (Valensi P et.al 1999) and "Obesity and the Activity of the Autonomic Nervous System" study by COLAK R et., al (Colak R et.al 2000).

CONCLUSION

In conclusion, the evaluation of obese young adults by simple non-invasive autonomic function tests provide diagnostic information about early subclinical cardiac autonomic dysfunction and is a useful tool to monitor the efficacy of therapeutic and lifestyle interventions.

Imprisoned in every fat man, a thin one is wildly signaling to be let out - Connolly, Cyril

Source of funding: self Conflict of interest: Nil

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ISSN : 0976-4550

INTERNATIONAL JOURNAL OF APPLIED BIOLOGY AND PHARMACEUTICAL TECHNOLOGY



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