Plasma Leptin Levels in Obese and Non-obese Confirmed Coronary Artery Disease in Patients of Khyber Pakhtunkhwa.

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Abstract: Obesity is associated with many metabolic and cardiovascular diseases; even moderate increase in BMI (Body mass index) is associated with increased risk of heart failure. Cardiovascular disease caused higher morbidity and mortality worldwide. Higher blood level of leptin is one of the factors depicting cardiovascular disease. Total 200 human subjects were recruited in the present study. Among these subjects 100 were angiographically assessed cardiac patients while 100 were normal healthy individuals who were taken as control. Our findings revealed that mean±SD plasma leptin level were higher in cardiac patients (17.57±4.39 ng/mL) as compared with control groups (6.82±3.05 ng/mL), with $p<0.000$ which was highly significant. Other clinical findings included mean±SD age (56.27±7.78 and 56.49±5.78 years), BMI (27.67±4.58 and 24.99±4.35 kg/m^2) were higher in female patients than male while lower in control group. Apo lipoprotein A (Apo A) (90.69±20.77 and 207.42±41.35mg/dL) were lower in patients than controls ($p<0.000$) while FBS (Fasting blood sugar) (109.22±47.52 and 89.03±12.59 mg/dL), and Apolipoprotein B (Apo-B) (99.39±26.63 and 81.21±24.56mg/dL) were higher in experimental group than in control group. The mean value of Total Cholesterol (TC) was (181.16±22.37 and 166.52±45.44 mg/dL), Triglycerides (TG) (166.91±63.28 and 136.83±26.13 mg/dL), and Low density lipoprotein (LDL-C) (mg/dL) (105.08±36 and 98.85±39.47), was higher in cases than control. HDL-C(mg/dL) (37.86±23.19 and52.93±33.58) was lower in cases than control group, whereas systolic B.P156.75±21.07 and 136.95±15.29 mmHg, diastolic B.P was93.15±10.43 and 85.58±8.10mmHg higher mean values were noted to be higher in experimental than control group respectively.
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Key Words: BMI, Leptin, Coronary Artery Diseases, Lipid Profile.

Introduction:

Obesity is associated with many metabolic and cardiovascular diseases, thereby contributing to increased morbidity and mortality, for example direct or indirect relation has been established between obesity and insulin resistance typeII diabetes, dyslipidedemia, inflammation, hypertension, stroke, atherosclerosis, and thrombosis (Lamon *et al.,* 1996, Kraus *et al.,* 1998).Even moderate increase in body mass index (BMI) is associated with increased risk of heart failure (Kenchaiah *et al.,* 2002). The association between obesity and coronary atherosclerosis has not been fully elucidated,it is believed that obesity is a strong risk factor for the development of coronary artery disease (CAD)(Lamon *et al.,* 1996, Kraus *et al.,* 1998, Kenchaiah *et al.,* 2002, Vischer *et al.,* 2001, Eckel *et al*., 2002). Obesity and overweight in adulthood are associated with large decrease in the life expectancy and increase in early death(Peters *et al.,* 2003). Leptin is a 16kDa protein consisting of 167 amino acids, is mainly synthesized by adipose tissue in proportion to adipose tissue mass (Faggioni *et al.,* 2001). Leptin was originally identified in 1994 by Friedman and considered to be the gene defect product that was responsible for obesity syndrome in mice. The gene was defined as ob, it is expressed exclusively in adipocytes (Soderberg *et al.,* 1999) and the obese mice carrying the mutation were called ob/ob mice (homozygous for spontaneous mutation in the ob gene) (Loffreda *et al*., 1998).

Theob gene is located on chromosome 7in humans. Leptin, the protein encoded by the ob gene, comes from the Greek word “leptose” means thin. A defect in leptin rendered to overeating and obesity, suggesting that leptin is a satiety factor. Circulating leptin levels are related to body fat mass, sex hormone levels, exposure to bacterial lipopolysaccharide, dietary fats and age. All these factors have also been correlated with increased vascular calcification, which is an emerging factor in the process of atherosclerotic vascular disease. Some studies have demonstrated the expression of leptin and its receptors in artery wall cells and a direct effect of leptin on osteogenic differentiation of a sub population of vascular cells called calcifying vascular cells (CVC)(Parihami *et al.,* 2001). In the present study we have hypothesized that

BMI is an independent predictor of coronary events in patients with known CAD. We studied patients with angiographically assessed cardiac patients and compared them with normal healthy subjects as controls.

Materials and Methods:

The present study was conducted at Post Graduate Medical Institute (PGMI), Lady Reading Hospital (LRH), Peshawar, Pakistan from June 2012 to May 2013. The study was approved from the Ethical Committee of PGMI, LRH, Peshawar. A total of 200 subjects were recruited in the present study on the basis of predefined selection criteria. All the subjects were divided into two main groups. One hundred subjects who were angiographically proved having coronary artery disease were grouped as patients, whereas the same number of subjects who were having no CAD or its symptoms and were apparently normal were placed in control group. All the subjects were examined for lipidprofile, Apo-A, Apo-B, fasting blood sugar (FBS) and serum leptin levels. Lipid profile was determined by calorimetric method using kitcat provided by Roche, Switzerland. Leptin was determined by enzymes immunoassay method where as Apo-A and Apo-B were determined by immune-turbidometric method utilizing kit supplied by Roche,Switzerland.

Result and Discussion:

A total of two hundred subjects were included in the present study, among these one hundred (n=100) were angiographically assessed cardiac patients and constitutedpatient's group while another one hundred(n=100) were normal healthy individuals of the same age, sex and socioeconomic status constituted control's group. The values of different parameters were expressed as mean±S.D and student "t" test and chi-square tests were used to compare the different variables in these groups.

General and biochemical characteristics of angiographically assessed cardiac patients and normal healthy individuals are depicted in table–1. This table shows mean±S.D age, BMIand other biochemical parameters of angiography confirmed patients and normal healthy individuals. As it is evident from the table that no significant change between the mean±SDage of patients and controls was notedwhere as this change was highly significant ($p< 0.001$) for mean±SD BMI of patients when compared with normal healthy individuals. It shows that serum leptin and obesity is strongly correlated with CAD. Our results are in agreement with these studies (Wolfgang *et al*., 2009, Justo *et al.,* 2007, Soderberg *et al.,* 2004, Wolk *et al.,* 2004, Robert *et al.,* 2003).The data further revealed various biochemical parameters, amongst these highly significant results were observed for FBS, Apo-A, Apo-B, and leptin for patients when compared with controls. Mean±SDFBS was found to 109.22±47.5 mg% in patients and it was 89.03±12.59 mg/dL in normal healthy individuals. Similarly mean±SD Apo-A, Apo-B and leptin in angiographically confirmed cardiac patients were noted to be 90.69±20.77 (mg/dL), 99.39±26.63 (mg/dL) and 17.57±4.39(ng/mL) as compared to normal healthy individuals who served as controls in whom it was observed to be 207.42±41.35 (mg/dL), 81.21±24.56 (mg/dL) and 6.82±3.05 (ng/mL)respectively.A similar trend in results ($p<0.001$) were observed for serum total cholesterol, triacylglycerides and HDL-C for patients when compared with controls. The results of the present study are in consistent with the previous studies (Efstratiadis *et al.,* 2007, Kamal *et al.,* 2004). The data furtherdemonstrated that systolic BP and diastolic BP ofangiographically assessed cardiac patients were found to be 156.75±21.07 mmHg and 93.15±10.43 mmHg respectively and were highly significant ($p<0.001$) when compared with normal healthy individuals in which it was observed to be 136.95±15.29 mmHg and 85.58±8.10 mmHg respectively (Table–1).

Table – 1: General and biochemical characteristics of angiographically assessed cardiac patients and normal healthy individuals (Controls).

Parameters	Patients (n=100)	Controls (n=100)	P – Value
	Mean±SD	Mean±SD	
Age (Years)	56.27±7.78	56.49±5.78	0.820
BMI (kg/m^2)	27.67±4.58	24.99±4.35	0.000
FBS (mg/dL)	109.22±47.52	89.03±12.59	0.000
APO-A (mg/dL)	90.69±20.77	207.42±41.35	0.000
APO-B (mg/dL)	99.39±26.63	81.21±24.56	0.000
Leptin (ng/mL)	17.57±4.39	6.82±3.05	0.000
T. Cholesterol (mg/dL)	181.16±22.37	166.52±45.44	0.004
TG (mg/dL)	166.91±63.28	136.83±26.13	0.000
LDL-C (mg/dL)	105.08±36.80	98.85±39.47	0.249
HDL–C (mg/dL)	37.86±23.19	52.93±33.58	0.000
Systolic B.P mm Hg	156.75±21.07	136.95±15.29	0.000
Diastolic B.P mm Hg	93.15±10.43	85.58±8.10	0.000

The table–2 shows frequency of study population on the basis of BMI. The data shows that maximum number of patients 48% were noted to be in over-weight group and these results were highly significant ($p<0.001$) when compared with normal healthy individuals. A significant result ($p<0.031$) was also observed for patients in obese group when compared

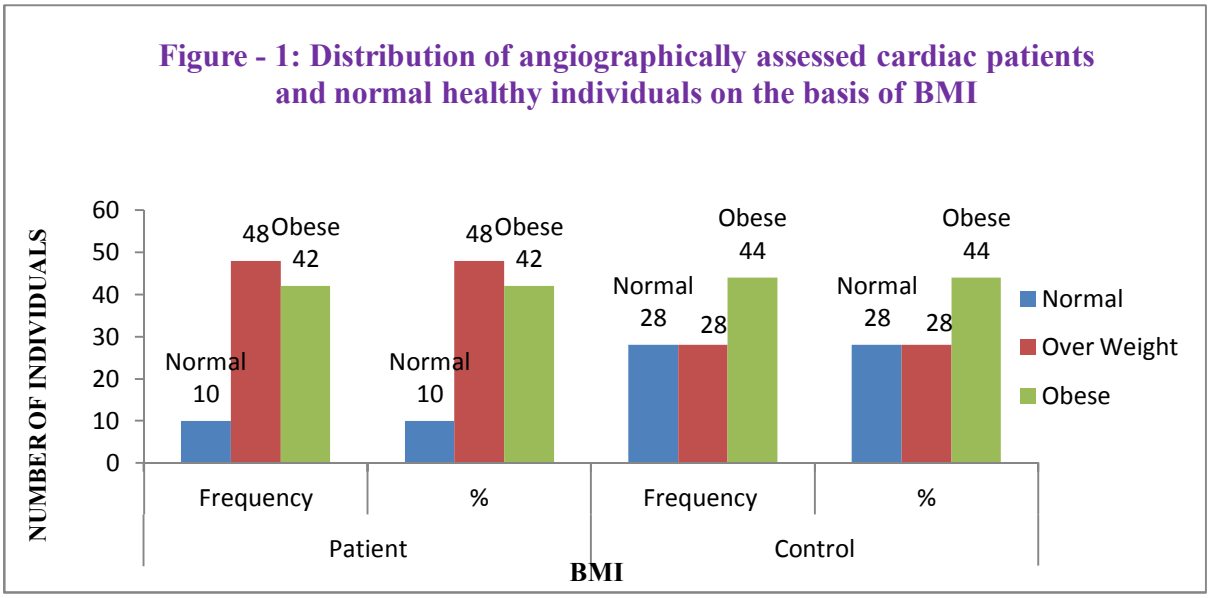
with controls.The data is graphically represented in Figure–1. Our findings are in agreement with the (Eckel *et al*., 2002, Parihami *et al.,* 2001, Soderberg *et al.,* 2004).The pattern of cardiac markers for angiographically assessed cardiac patients and controls are depicted in table–3. These markers are Apo-A, Apo-B, and serum leptin.The data for Apo-A showed that the maximum number of patients (93%) were found in abnormal range and result were highly significant ($p<0.000$) when compared with normal individuals. For Apo-B the data showed that maximum number of patients (52%) fall in normal range but the results were again significantly higher ($p<0.000$) when compared with controls. And for plasmaleptin levels table-3 further showed that maximum number of angiographically assessed patients (76%) were found to be in abnormal range and a highly significant ($p<0.000$) result was obtained when compared with controls. The same is represented graphically in Figure–2 respectively. Similar trends of result were observed in studies carried out elsewhere (Robert *et al.,* 2003, Wallace *et al*., 2001).

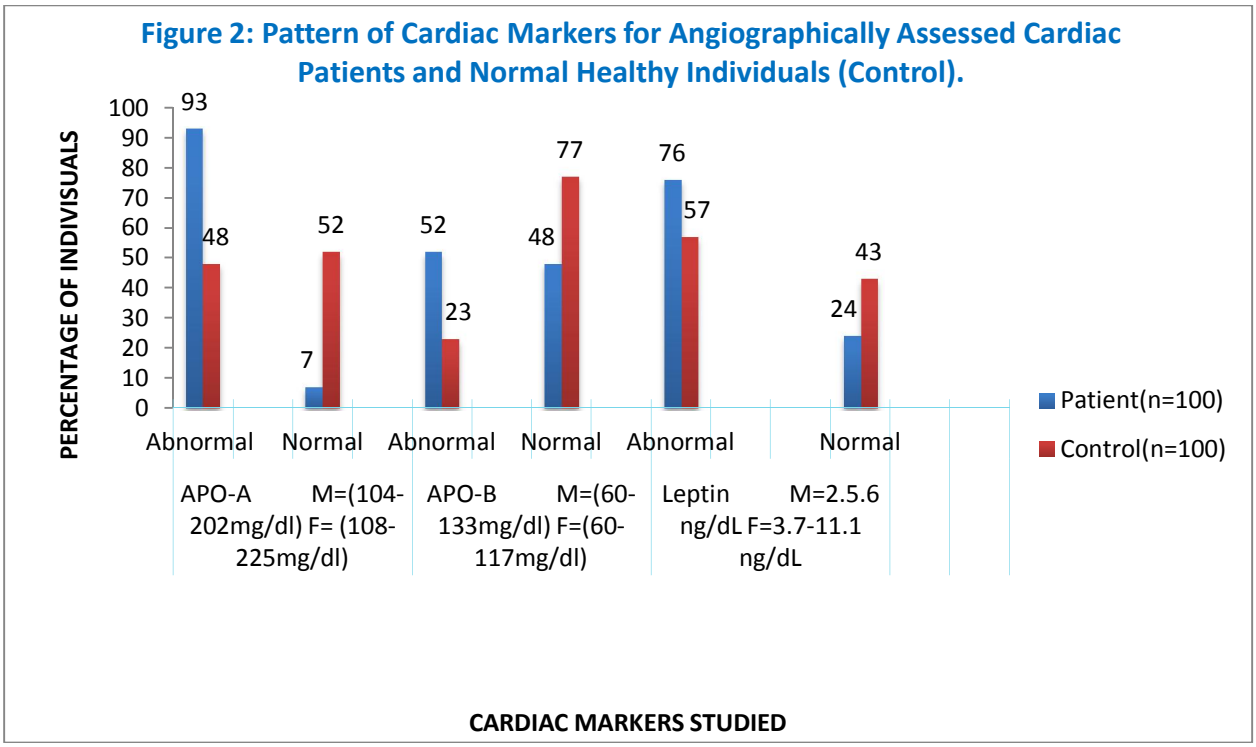
Table – 2: Distribution of Angiographically Assessed Cardiac Patients and Normal Healthy Individuals on the basis of BMI

BMI	Patients		Control		Chi.Sq	P–Value
	Frequency	%	Frequency	%		
Normal	10	10.0	28	28.0	Referent	
Over-Weight	48	48.0	28	28.0	12.32	0.000
Obese	42	42.0	44	44.0	4.60	0.031

Table – 3: Pattern of Cardiac Markers for Angiographically Assessed Cardiac Patients And Normal Healthy Individuals

APO		Patient(n=100)	Control(n=100)	Chi.Sq	P-Value
APO-A M=(104-202mg/dL) F= (108-225mg/dL)	Abnormal	93	48	1.225	0.001
	Normal	7	52		
APO-B M=(60-133mg/dL) F=(60-117mg/dL)	Abnormal	52	23	26.593	0.085
	Normal	48	77		
Leptin M=2.0-5.6 ng/dL F=3.7-11.1 ng/dL	Abnormal	76	57	55.339	0.001
	Normal	24	43		





Conclusion:

Increases BMI as well as plasma leptin levels are associated independently with acute coronary syndromes, in that they increase the risk for myocardial infarction or unstable angina in subjects with known CAD. These effects are independent of all other traditional established cardiovascular and metabolic diseases, such as insulin resistance and dyslipidemia. These findings may have important implications both for knowing the decreased life expectancy associated with obesity as well as for the clinical management of patients with coronary syndromes. It is further suggested that the number of subjects should be increased and the study should be extended to waste area for more accurate and authentic findings.

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