



ROLE OF CARDIAC MARKERS IN CENTRAL OBESITY IN POPULATION OF PUNJAB

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ABSTRACT

Obesity is defined as an excessively high amount of body fat or adipose tissue in relation to lean body mass. Men and women with BMI $\geq 30\text{kg/m}^2$ are considered as obese and are generally at higher risk for adverse health events than overweight individuals (BMI = 25.0 – 29.9 kg/m²) or lean (BMI Between 18.5 and 24.9 kg/m²). The objective of the study was to determine the link between central obesity and cardiovascular diseases (CVD) using cardiac markers in the population of Punjab. The present prospective study was undertaken in the Medicine and Biochemistry departments of SGRDIMSAR, Amritsar. Fasting blood samples were drawn from 40 subjects and sent for biochemical analysis. BMI has a positive and highly significant correlation with waist circumference (WC) at $p \geq 0.01$. WC is negatively and significantly correlated with HDL and Nitric Oxide at $p \geq 0.05$. A significant correlation is observed between Cholesterol and Triglycerides $p \geq 0.05$ and highly significant correlation is observed between cholesterol, HDL and LDL levels with $p \geq 0.01$. Nitric oxide has positive correlation with Lipoprotein and a highly significant correlation with homocysteine at $p \geq 0.01$. Myoglobin has a positive correlation with waist circumference at $p \geq 0.05$. So the cardiac Markers may prove useful for early identification of susceptible obese individuals who are at high risk of developing CVD.

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INTRODUCTION

Obesity is a type of nutritional disorder due to imbalance between energy intake and energy expenditure resulting in positive energy balance, resulting in an increase in the body weight to the extent of 20% or more of the standard weight. Obesity epidemic results in substantial decrease in the quality of life, life expectancy and it accounts for heavy expenditure in provision of health care.¹ A central or an abdominal obesity is an important risk factor for cardiometabolic diseases, including type 2 diabetes, hypertension, dyslipidemia and coronary heart disease.^{2,3} Framingham Heart Study was the first epidemiological studies to demonstrate the association between obesity and cardiovascular disease.⁴ there are following Indices to determine body fat distribution: Visceral abdominal fat, subcutaneous abdominal fat and pericardial fat.^{5, 6} Assessment of weight and body fat is done using Body Mass Index (BMI): (weight (kg)/height (m²), waist circumference (WC), waist-to-height ratio (WHR) and Skin fold.

Men and women with BMI $\geq 30\text{kg/m}^2$ are considered as obese and are generally at higher risk for adverse health events than overweight individuals (BMI = 25.0 – 29.9 kg/m²) or lean (BMI Between 18.5 and 24.9 kg/m²).

Therefore, BMI has become the “gold standard” for identifying patients at increased risk of adiposity related adverse health outcomes.⁷ Excess abdominal fat (android/upper body/central) is directly associated with diabetes and cardiometabolic diseases.⁸ Therefore, WC is often used as a surrogate marker of abdominal fat mass.⁹ Men ≥ 102 cm (≥ 40 in.) and women ≥ 88 cm (≥ 35 in.) are at high risk of cardiometabolic syndrome in terms of WC.¹⁰ The present study was carried to categorize obese and non obese individuals by means of their waist circumference as a marker and to determine the link between central obesity and cardiovascular diseases using cardiac markers in the population of Punjab.

MATERIAL AND METHODS

This study was undertaken in the Medicine and Biochemistry departments of the Sri Guru Ram Das Institute of Medical Sciences And Research, Vallah, Amritsar. Total 40 subjects were taken who approached medicine OPD between May - July 2017 and were categorised into two groups: 20 healthy obese females (waist circumference ≥ 88 cm (≥ 35 in.) and 20

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healthy obese males (waist circumference ≥ 102 cm (≥ 40 in.)). Written Informed consent was taken from all the subjects. Patients with Diabetes Mellitus and with history of acute infections established cardiovascular events, tuberculosis, gout, rheumatoid arthritis and skeletal muscle injury, renal failure, thyroid diseases, pregnant women and those taking antioxidants were excluded from the study. A detailed personal history including food habits, physical activities was obtained in the form of questionnaire. Clinical examination included waist circumference, weight, height, BMI, ratio and blood pressure using weighing machine, measuring tape, height chart, stethoscope and sphygmomanometer. Waist circumference was taken at the midpoint between the lowest rib and the iliac crest after the patient exhaled while standing without shoes, both feet touching and arms hanging freely with the measuring tape placed perpendicular to the long axis of the body and horizontal to the floor. Fasting blood sample was drawn and sent for biochemical analysis of serum lipid profile, serum myoglobin, serum homocysteine, serum nitric oxide and serum lipoprotein (a). Serum lipid profile was estimated on fully autoanalyzer Siemens Dimension RxL, serum myoglobin was estimated by Vitreous 5600 integrated system by ortho-clinical diagnostics, serum homocysteine was

estimated by chemiluminescence Siemens Immulyte 2000Xpi, HbA1C, and serum nitric oxide was estimated by ELISA method by Erba, serum lipoproteins were estimated by semiautoanalyzer Erba5Transasia. Thereafter data was statistically analysed by Pearson's correlation analysis using SPSS version 17.

OBSERVATIONS AND RESULTS

RESULTS

- BMI was negatively correlated with all parameters except waist circumference and myoglobin and had a positive and highly significant correlation with waist circumference at $p \geq 0.01$
- Waist circumference was negatively and significantly correlated with HDL and nitric oxide at $p \geq 0.05$. The waist circumference increased with a decrease in HDL levels, while an increase in WC was seen with an increase in lipid profile.

Table 1

Gender	Number	Age (Mean \pm SE)	Height (Mean \pm SE)	Weight (Mean \pm SE)	BMI (Mean \pm SE)	WC (Mean \pm SE)
	40	43.90 \pm 1.55	159.73 \pm 1.32	83.43 \pm 1.82	32.72 \pm 0.65	41.90 \pm 0.46
Male	20	42.89 \pm 2.67	166.03 \pm 1.59	90.05 \pm 1.75	32.85 \pm 0.94	43.42 \pm 0.34
Female	20	44.81 \pm 1.75	154.02 \pm 1.02	77.43 \pm 2.47	32.60 \pm 0.92	40.52 \pm 0.69

Table 2

Gender	Number	Cholesterol (Mean \pm SE)	Triglyceride (Mean \pm SE)	HDL (Mean \pm SE)	LDL (Mean \pm SE)	VLDL (Mean \pm SE)
	40	185.03 \pm 5.71	204.83 \pm 13.56	41.85 \pm 1.29	119.18 \pm 4.32	39.36 \pm 2.47
Male	20	179.63 \pm 10.11	228.95 \pm 18.87	38.89 \pm 1.77	115.63 \pm 7.27	45.47 \pm 3.79
Female	20	189.90 \pm 5.95	183.00 \pm 18.52	44.52 \pm 1.70	122.38 \pm 5.00	33.55 \pm 2.69

Table 3

Gender	Number	Homocysteine (Mean \pm SE)	Nitric Oxide (Mean \pm SE)	Lipoprotein (Mean \pm SE)	Myoglobin (Mean \pm SE)
	40	79.91 \pm 24.59	5627.06 \pm 1085.29	13.44 \pm 2.30	54.91 \pm 8.76
Male	20	93.68 \pm 34.89	4210.92 \pm 1246.32	10.86 \pm 1.77	72.68 \pm 17.42
Female	20	67.46 \pm 35.21	6908.33 \pm 1713.83	15.76 \pm 4.07	38.82 \pm 3.24

Table 4

		BMI	WC	Cholesterol	Triglyceride	HDL	LDL	VLDL	Homocysteine	Nitric Oxide	Lipoprotein	Myoglobin
BMI	Correlation	1	.434**	-.230	-.170	-.249	-.151	-.251	-.088	-.250	-.009	.074
	Sig (2 Tailed)		.005	.154	.295	.121	.351	.124	.591	.119	.956	.649
WC	Correlation	.434**	1	.015	.075	-.402*	.132	.141	-.086	-.376*	-.116	.243
	Sig (2 Tailed)	.005		.926	.647	.010	.416	.391	.599	.017	.475	.130
Cholesterol	Correlation	-.230	.015	1	.344*	.448**	.937**	.294	-.131	-.121	-.106	.151
	Sig (2 Tailed)	.154	.926		.030	.004	.000	.069	.420	.456	.515	.353
Triglyceride	Correlation	-.170	.075	.344*	1	-.034	.139	1.000**	-.055	.031	-.083	.243
	Sig (2 Tailed)	.295	.647	.030		.835	.391	.000	.736	.848	.612	.130
HDL	Correlation	-.249	-.402*	.448**	-.034	1	.252	-.135	-.103	.131	-.038	-.240
	Sig (2 Tailed)	.121	.010	.004	.835		.116	.412	.529	.420	.816	.135
LDL	Correlation	-.151	.132	.937**	.139	.252	1	.142	-.118	-.181	-.070	.186
	Sig (2 Tailed)	.351	.416	.000	.391	.116		.388	.469	.265	.669	.250
VLDL	Correlation	-.251	.141	.294	1.000**	-.135	.142	1	-.079	.083	-.036	.314
	Sig (2 Tailed)	.124	.391	.069	.000	.412	.388		.632	.616	.828	.051
Homocysteine	Correlation	-.088	-.086	-.131	-.055	-.103	-.118	-.079	1	.436**	-.216	-.055
	Sig (2 Tailed)	.591	.599	.420	.736	.529	.469	.632		.005	.180	.735
Nitric Oxide	Correlation	-.250	-.376*	-.121	.031	.131	-.181	.083	.436**	1	.057	-.134
	Sig (2 Tailed)	.119	.017	.456	.848	.420	.265	.616	.005		.727	.409
Lipoprotein	Correlation	-.009	-.116	-.106	-.083	-.038	-.070	-.036	-.216	.057	1	-.078
	Sig (2 Tailed)	.956	.475	.515	.612	.816	.669	.828	.180	.727		.632
Myoglobin	Correlation	.074	.243	.151	.243	-.240	.186	.314	-.055	-.134	-.078	1
	Sig (2 Tailed)	.649	.130	.353	.130	.135	.250	.051	.735	.409	.632	

*Correlation significant at 0.05 level
 **Correlation significant at 0.01 level

- Cholesterol was positively correlated with most of the parameters. A significant correlation was observed between cholesterol and triglycerides at $p \geq 0.05$ and highly significant correlation was observed between cholesterol, HDL and LDL levels with $p \geq 0.01$.
- Triglycerides showed a similar positive correlation with most of the parameters. A significant correlation of triglycerides with cholesterol at $p \geq 0.05$ and highly significant correlation with VLDL was observed at $p \geq 0.01$.
- HDL had a negative correlation with most parameters as a decrease in this parameter was responsible for an increase of other parameters. A significant negative correlation with waist circumference at $p \geq 0.05$ and a highly significant positive correlation with cholesterol at $p \geq 0.01$ was observed.
- LDL had a positive and highly significant correlation with cholesterol at $p \geq 0.01$. It showed positive correlation with most of the parameters.
- VLDL had a positive correlation with most of the parameters. It showed a highly significant and positive correlation with triglycerides at $p \geq 0.01$.
- Homocysteine was negatively correlated with all the parameters except nitric oxide. A highly significant and positive correlation was observed with nitric oxide at $p \geq 0.01$.
- Nitric oxide had a significant and negative correlation with waist circumference at $p \geq 0.05$, while a positive and highly significant correlation was observed with homocysteine at $p \geq 0.01$.
- Lipoprotein was negatively correlated with all the parameters except nitric oxide. Lipoproteins and nitric oxide showed positive correlation.

DISCUSSION

In today's world the prevalence of obesity and overweight is reaching epidemic levels¹¹. Morbidity and Mortality due to obesity induced diseases are increased as a result of high obesity incidence¹². Body fat distribution is also an important risk factor for obesity related diseases. Miyawaki *et al*¹³ in cross sectional experiment on 955 subjects confirmed the relation between (visceral abdominal fat) VAF and atherosclerosis risk factor comprising hyperlipidemia and blood sugar. Excess body fat (also known as central or upper body fat) is associated with an increased risk of cardiometabolic disease. However, precise measurement of Subcutaneous abdominal adipose tissue (SAAT) and intra abdominal adipose tissue (IAAT) requires the use of expensive radiological imaging techniques like MRI and CT. Therefore, WC is often used as a surrogate marker of abdominal fat mass and is associated with cardiometabolic disease risk¹⁴. Wang *et al*⁹ reported that men and women who have WC greater than 40 inches (102 cm) and 35 inches (88 cm) respectively are considered to be at increased risk for cardiometabolic disease. These cut points were derived by Lean¹⁵ from a regression curve that identified the waist circumference values associated with a BMI ≥ 30 Kg /m² in primarily Caucasian men and women living in north Glasgow. This is in accordance with our study where WC of men was in the range of 40- 46 (Mean 43.42 \pm 0.34 cms), of women was in the range of 37 – 49 (Mean 40.52 \pm 0.69 cms) and BMI was 32.72 \pm 0.65 (Table 1). BMI has a positive and highly significant correlation with waist circumference at $p \geq 0.01$ (Table 5). Ruel *et al*¹⁶ stated that

an increase in waist circumference or BMI was associated with a significant reduction in HDL. This is in accordance with our study where WC is negatively correlated with HDL. HDL has a significant negative correlation with waist circumference at $p \geq 0.01$ (Table 5).

Table 5

Variables	Male (n=19) Mean \pm SD	Female (n=21) Mean \pm SD	p- value
Age (years)	42.89 \pm 11.66	44.81 \pm 8.02	0.553
Height (cm)	166.03 \pm 6.91	154.02 \pm 4.65	0.001
Weight (kg)	90.05 \pm 7.63	77.43 \pm 11.30	0.001
BMI (kg/m ²)	29.80 \pm 5.84	25.66 \pm 7.24	0.053
WC (inches)	43.42 \pm 1.46	40.52 \pm 3.19	0.001
Serum Cholesterol (mg/dl)	179.63 \pm 63	189.90 \pm 27.25	0.388
Serum Triglycerides (mg/dl)	228.95 \pm 95	183.00 \pm 84.86	0.091
HDL (mg/dl)	38.89 \pm 7.72	44.52 \pm 7.81	0.028
LDL (mg/dl)	115.63 \pm 31.68	122.38 \pm 22.94	0.442
VLDL (mg/dl)	45.47 \pm 16.51	33.55 \pm 12.02	0.013
Homocysteine (ng/ml)	93.68 \pm 152.07	67.46 \pm 161.37	0.601
Serum Nitric acid	4210.92 \pm 5432.58	6908.33 \pm 7853.78	0.219
Lipoprotein (ng/ml)	10.86 \pm 7.72	15.76 \pm 18.66	0.294
Myoglobin (ng/ml)	72.68 \pm 75.93	38.38 \pm 14.84	0.052

Individuals having higher levels of triglycerides are more prone to CVD. Van Pelt *et al*¹⁷ in his study on postmenopausal women at Washington University School of Medicine tested the sensitivity of waist circumference (central adiposity) as an index of disease risk and stated that excess waist size had a strong association with hypertriglyceridemia than body mass. In our study, triglycerides show a similar positive correlation with most of the parameters (Table 4).

Leo *et al*¹⁸ in their study on 104 patients free of known metabolic diseases demonstrated a strong association between body fatness and elevated serum Cholesterol and serum triglyceride levels. Grundy *et al*¹⁹ reported that overproduction of VLDL contribute to hypertriglyceridemia. Nestel²⁰ described the striking relationship between VLDL and HDL metabolism as an inverse association between their respective removal rates. In our study, a significant correlation of triglycerides with cholesterol is observed at $p \geq 0.05$ and highly significant correlation with VLDL at $p \geq 0.01$ (Table 5).

Berchtold *et al*²¹ in their study on 1332 patients with different degrees of obesity reported that HDL cholesterol levels were decreased in obese patients. This is in accordance with our study where we observed that HDL has a highly significant positive correlation with cholesterol at $p \geq 0.01$. Obesity and Serum LDL are important risk factors of CVD. Luo *et al*²² in their study on 1538 subjects reported that obese subjects (BMI ≥ 25 Kg/m²) had significantly higher serum LDL levels than the lean subjects (BMI < 25 Kg/m²). In the present study LDL has a highly significant positive correlation with cholesterol at $p \geq 0.01$ (Table 4).

Nitric oxide (NO) is a potent regulator of vasomotor tone and an important antiatherogenic molecule. Elahi *et al*²³ stated that these antiatherogenic effects include the regulation of endothelium dependent vasodilatation, inhibition of smooth muscle cell proliferation and modulation of cellular interactions by inhibiting cell adhesion. Supporting the previous numerous studies we observed higher NO levels in obese individuals. Kondo *et al*²⁴ determined the relationship between abdominal circumference and concentration of NO in 339 women and stated that a reduction in NO bioactivity occurs with abdominal fat accumulation in women. In our

study, Nitric oxide has a significant and negative correlation with waist circumference at $p \geq 0.05$ (Table 4).

Homocysteine is considered as an emerging cardiovascular risk factor. Atanassova *et al*²⁵ postulated that hyperhomocysteinaemia participates in pathogenesis of ischaemic stroke. Mahalle *et al*²⁶ in their study in 300 Indian subjects with proven coronary heart disease, homocysteine was found to be positively associated with TG and VLDL and negatively with HDL. Tyagi *et al*²⁷ reported a decreased NO bioavailability and disturbed vasodilation with hyperhomocysteinemia. Unver *et al*²⁸ concluded a positive correlation between homocysteine and NO ($p=0.001$) similar to our study where we have observed positive and highly significant correlation between homocysteine and NO at $p \geq 0.01$ (Table 4).

Lipoprotein LP (a) has been added to the list of independent risk factors for CVD whose incidence is greater in obese subjects. Donatelli *et al*²⁹ in their study on obese individuals reported a significant positive correlation between LP (a) levels and glucose could be revealed ($p < 0.05$). Tektas *et al*³⁰ investigated the possible effects of Serum Lipoprotein associated phospholipase A2 (Lp-PLA2) mass levels on Arginase/ Nitric oxide (NO) pathway and concluded that Lp-PLA2 levels were found to be positively correlated with Arginase and negatively related with total nitrite levels. Present study observed a positive correlation of Lipoproteins with nitric oxide (Table 4). Kanner *et al*³¹ stated that when no concentration increase, total oxygenated myoglobin (MbO₂) concentration decreases and also ferric Mb (MetMb) formation increases. Unver *et al*²⁸ detected myoglobin together with NO in high levels in obese individuals ($p=0.001$) similar to our study where myoglobin shows a positive correlation with nitric oxide at $p \geq 0.05$ (Table 4).

The data obtained by studying lipid profile (Cholesterol, Triglycerides, HDL, LDL, VLDL) along with cardiac markers i.e. Lipoprotein (a), Homocysteine, Nitric oxide and Myoglobin can be useful in treatment and prediction of the prognosis of obesity in addition with other studies.

CONCLUSION

Obesity is a worldwide disease causing a number of medical and psychological problems resulting from combination of higher energy intake and sedentary life style. The present study concluded that increased waist circumference was directly related with increase in levels of Cholesterol, Triglycerides, LDL, VLDL, Myoglobin and decrease in HDL levels. Therefore, it was emphasized to understand the importance of metabolic profile in central obesity responsible for the higher risk of cardiovascular events.

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