

Correlation of Lipid Indices in Obese Diabetic and Nondiabetic Subjects

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Abstract

Aim :- To study correlation of lipid indices in obese individuals with and without diabetes mellitus disease

Background :- In view of changing lifestyle and urbanization the prevalence of Diabetes Mellitus and Obesity are increasing and seem to go hand in hand. Both disorders have similar sequelae viz. Hypertension, Cardiovascular disease, Stroke and other vascular diseases. Instead monitoring lipid profile directly to assess risk of atherosclerosis, the present trend was to estimate lipid indices / atherogenic indices as these ratios are altered inspite of normal range of different Lipoproteins.

Material and Methods:- The study was done in GGH, Guntur from August 2019 to February 2020. 100 obese male and female subjects in the age group of 20 -65 yrs were selected for the present study, both diabetic and nondiabetic (50 each). Similarly 50 age and sex matched lean, nondiabetic individuals were selected as controls. Written informed consent was obtained from all the subjects to participate in the study. Anthropometric data was recorded for all the subjects and Blood samples were collected to analyse FBS, PPBS, TC, Tg, HDL-C, LDL-C & VLDL-C.

Results :- Atherogenic indices - atherogenic index of plasma (AIP), Castelli's risk index-1(CRI-1), Castelli's risk index-2 (CRI-2) and small, dense Low Density Lipoprotein (sdLDL)- were calculated from lipid profile values. BMI was calculated from Height and weight. Paired Student's 't' test found to be statistically significant for BMI (p-value <0.00001), AIP (P-value < 0.001) and CRI-1 (P-value <0.01) in diabetic and nondiabetic individuals compared to controls. Whereas CRI-2 in diabetics was not correlated with either nondiabetics or controls. Similarly one-way ANOVA of three groups showed obesity per se leads to atherogenicity with or without diabetes. CRI-2 (P value <0.07) in the one-way ANOVA did not prove correlation between HDL-C and LDL-C. sdLDL showed significant difference in Diabetic Obese individuals compared to nondiabetics and controls.

Conclusion:- Lipid profile and BMI were warning signs of obesity for the forthcoming health hazards like Hypertension or CVD. But estimation of lipid indices (ratios) would surely indicate degree of probability of atherogenesis.

Key words: Obesity, Lipid indices, atherogenesis

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I. Introduction

Obesity is defined as abnormal or excessive fat accumulation. It is a serious health issue involving all age groups. It is expressed in terms of Body Mass Index (BMI). BMI of more than 25.0 is considered as overweight and above 30.0 is Obese in Asians. BMI is defined as a person's weight in Kilograms divided by the square of his height in meters. Changes in lifestyle, urbanization and stress are leading causes of Obesity apart from genetic transmission. According to National Family Health Survey, India (NFHS)-2014 1.9 billion adults (18yrs and older) were overweight.¹ As mentioned by NFHS, -3 13% were women (15-49yrs) and 9% were men (15-49yrs).² In addition, 44% of the Diabetes burden is conferred to be due to obesity. The prevalence of obesity was less in persons involved in agriculture and manual work.

Abdominal fat distribution or android obesity proved hazardous than gynoid fat distribution or even distribution of fat all over the body.³

Obesity is associated with dyslipidemia which leads to cardiometabolic diseases. Pathophysiology of dyslipidemia in obesity is over production of VLDL, increased release of Free Fatty Acids from adipocytes into circulation and transportation to liver and formation of sdLDL. Dyslipidemia commonly presents as Hypercholesterolemia, hypertriglyceridemia, lowered HDL-C and high LDL-C. The situation is almost same in Type 2 Diabetes Mellitus (DM), where dysfunctioning of lipoprotein lipase aggravates the situation.⁴

As defined by National Cholesterol Education Programme (NCEP) Adult Treatment Panel -III the Normal values were as follows: Serum Total Cholesterol <200mg/dl , Serum Triglycerides <150mg/dl , Serum High Density Lipoprotein (HDL-C) >40mg/dl and Serum Low Density Lipoprotein (LDL-C) <130mg/dl.

In both obesity and Diabetes Mellitus mere absence of dyslipidemia does not rule out microvascular changes. In such an event Lipid indices like atherogenic Index of Plasma(AIP) , Castelli's Risk Index-1 (CRI-1) and Castelli's Risk index-2(CRI-2) give an insight into the atherogenic status of the individual.⁵

AIP acts as a surrogate marker of apolipoprotein(B) , and it accurately reflects the status of atherogenic LDL-C and antiatherogenic HDL-C.(Ref)

Castelli's risk index -I (TC/HDL-C) indicates intima-media thickness in carotid arteries and higher values are associated with coronary plaque formation⁶

Low Density Lipoprotein has 3 subclasses according to size and density. Large(buoyant) - 26.0-28.5nm, Intermediate - 25.5 - 26.4nm and Small , dense LDL-24.2 -25.5nm were 3 subclasses .⁷These phenotypes can be segregated by HPLC, GGE(Gradient Gel Electrophoresis) and NMR(Nuclear Resonance Imaging). LDL particles can be modified by CETP (Cholesterol Ester Transfer Protein) . CETP mediates exchange of Tgs and CE(Cholesteryl Esters) between LDL and VLDL and HDL. This leads to production of subclasses of LDL. Circulation time of sdLDL was longer. It was shown that native LDL does not cause lipid accumulation and atherogenic plaque formation , but modified LDL like glycated, desialylated or oxidized LDL are highly atherogenic.

Smaller size of sdLDL favours its penetration into arterial wall and longer circulation time increases atherogenic modifications.. Hence in our study sdLDL was included along with other lipid indices. The ratio of Tg to HDL-C considered as substitute to sdLDL concentration in plasma.⁸

A Fasting Blood Glucose value of >126mg/dl or Random Blood Glucose value of >200mg/dl were considered as diabetes according to ICMR guidelines 2018.

The present study was conducted with an aim to assess the significance of Lipid indices in obese individuals with or without Diabetes who are at risk developing coronary artery disease.

II. Material and Methods

The study was conducted between April 2019 and obtaining informed consent. 50 individuals were obese diabetics (known cases) , 50 individuals were obese nondiabetics (diabetes ruled out from their FBS values) and 50 age and sex matched controls ,were nondiabetic lean persons. Fasting venous blood samples 5ml were collected from all subjects under aseptic conditions. The samples were analyzed in VITROS250 Autoanalyzer by enzymatic methods using dry chemistry reagent slides for FBS, Urea, Creatinine and Lipid profile which included TC, Tg, HDL-C, & VLDL-C . LDL-C was calculated using Friedwald's formula.

Lipid indices were calculated using relevant formulae.

1. Atherogenic Index of Plasma (AIP) = $\text{Log}(\text{Tg}/\text{HDL-C})$
2. Castelli's Risk Index-1 = $\text{TC}/\text{HDL-C}$
3. Castelli's Risk Index-2 = $\text{LDL-C}/\text{HDL-C}$
4. Small, Dense Low Density Lipoprotein(sdLDL) = $\text{Tg}/\text{HDL-C}$
5. Anthropometric data was recorded for all subjects like height, weight abdominal circumference and blood pressure.All the subjects were normotensive.

Statistics was done using NCSS v20.0.3 software. All the values are expressed as Mean± SD. Paired Student's 't' test performed at 95% confidence interval at significance value of <0.05 for continuous variables. ANOVA was done to understand correlation between groups and within groups

Exclusion criteria :-Thyroid disease, Cushing's syndrome, Renal disease, Heart disease, Pregnancy and Family history of Obesity. Individuals on medication for epilepsy, Oral contraceptive pills & antipsychotics were excluded

Inclusion criteria :- BMI(Body mass index) of more than 30.0 calculated from height and weight as Obese and less than 25.0 as normal(WHO Classification).

III. Results

In the present study, females were included more than males. 73.9% were diabetics and 26% were nondiabetics. Amongst the 150 individuals included in the study 46% have high Tg levels and low HDL-C values.

The present study was done to evaluate the influence of Diabetes Mellitus on Obesity related health issues. Lipid indices were considered to assess health risk rather than Lipid profile parameters directly. BMI was found to be significantly higher in the study group (Mean±SD 39.65±6.85, 36.79±6.65) compared to controls(26.41±4.76).

FBS vale of less than 126mg/dl was considered as nondiabetic (WHO guidelines). Oneway ANOVA of different ratios - AIP, CRI-1, CRI-2 and sdLDL between the three groups showed significant risk as indicated

by AIP, CRI-1 and sdLDL (P values <0.001, <0.003 & <0.0001 respectively) . But the risk is not significant as indicated by CRI-2, LDL- C/HDL-C ratio (P value <0.07).(Table-2)

Table -1 Mean and SD values of BMI and Lipid indices in three groups

Subject		FBS	BMI	AIP	CRI-1	CRI-2	sdLDL
Obese Diabetic ects N=50	Subj Mean ±Std.Dev	152.01 ± 44.72	39.65 ± ±6.85	0.28 ± ±0.32	4.68 ± ±1.13	3.04 ±1.02	5.79 ±4.4
Obese Nondiabetic ects N=50	Subj Mean ±Std.Dev	93.95 ± 15.45	36.79 ± ±6.65	0.26 ± ±0.21	4.71 ± ±1.29	2.97 ±1.00	3.81 ±1.54
Controls N=50	Mean ±Std.Dev	98.71 ± 9.98	26.41 ± ±4.76	0.46 ± ±0.37	5.71 ±2.4	3.51 ±1.68	7.61 ±3.01

Table -2 Oneway ANOVA of lipid indices in Diabetic Obese individuals , Onodiabetic Obese individuals and Controls (N=50 in each group)

Parameter	F-ratio	P-Value	Significance
BMI	64.975	<0.00001	High
AIP	6.839	<0.001	High
CRI-1	5.896	<0.003	High
CRI-2	2.674	<0.07	NOT significant
sdLDL	17.596	<0.0001	High

In the study groups there was male preponderance in Nondiabetic obese individuals. In the Nondiabetic obese individuals there was significant correlation between males & females for BMI and CRI-1 (TC/HDL-C ratio) as shown in Table -3 (P-value <0.02 & <0.006 respectively) That means high TC values are salient feature of Obesity irrespective of diabetes status. Similarly in diabetic obese individuals none of the ratios showed any correlation between males and females as indicated by oneway ANOVA -Table 4.

All the lipid ratios (AIP, CRI-1, CRI-2 and sdLDL) were on the high end in Obese diabetic individuals compared to controls as indicated by the Paired Student's "t" test - Table-5 (P-values <0.009, <0.002, <0.03 & <0.006 respectively). The same was proved in Obese nondiabetic individuals as shown in Table -6 with P-values <0.001, <0.01, <0.0001 for AIP, CRI-1 and sdLDL. High LDL-C /HDL-C ratio was not found in Obese Nondiabetic individuals compared to controls (P-value of CRI-2 <0.06)

Table -3 Oneway ANOVA of lipid indices between males and females in Nondiabetic Obese individuals (Males 18 number & Females 32 number)

Parameter	Gender	N	Mean d.Dev	± St	F-ratio	P-value	Significance
BMI	♂	31	38.23±6.35		5.520	<0.023	SIGNIFICANT
	♀	19	42.32±5.29				
AIP	♂	31	0.32±0.31		0.431	<0.515	NOT Significant
	♀	19	0.26±0.32				
CRI-1	♂	31	5.05±0.93		8.13	<0.006	SIGNIFICANT
	♀	19	4.19±1.19				

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CRI-2	♂	31	3.2±0.84	1.50		
	♀	19	2.84±1.24		<0.227	NOT Significant
sdLDL	♂	31	6.33±4.96	1.23		
	♀	19	4.91±3.23		<0.27	NOT Significant

Table-4 :- Oneway ANOVA of Lipid Indices in males (♂) and females (♀) in Obese diabetic subjects

Parameter	Gender	N	Mean td.Dev	± S	F-ratio	P-value	Significance
BMI	♂	18	35.84±5.67		0.579		
	♀	32	37.33±7.17			<0.45	NOT SIG
AIP	♂	18	0.30±0.22		1.395		
	♀	32	0.23±0.19			<0.24	NOT SIG
CRI-1	♂	18	4.75±1.22		0.025		
	♀	32	4.69±1.34			<0.88	NOT SIG
CRI-2	♂	18	3.14±0.97		0.775		
	♀	32	2.88±1.01			<0.38	NOT SIG.
sdLDL	♂	18	4.09±1.97		0.613		
	♀	32	3.73±1.25			<0.43	NOT SIG.

Table 5 :- PAIRED STUDENT'S "t" TEST DIABETIC OBESE INDIVIDUALS Vs CONTROLS

PARAMETER	SEM	P-VALUE	SIGNIFICANCE
BMI-diabetics controls	0.968 0.672	<0.00001	HIGHLY SIGNIFICAANT
AIP-diabetics controls	0.046 0.052	<0.009	HIGHLY SIGNIFICANT
CRI-1- diabetics controls	0.159 0.339	<0.002	SIGNIFICANT
CRI-2 - diabetics controls	0.144 0.237	<0.03	SIGNIFICANT
SdLDL - diabetics controls	0.622 0.217	<0.006	SIGNIFICANT

Table-6 :- PAIRED STUDENT'S "t" TEST NONDIABETIC OBESE INDIVIDUALS Vs CONTROLS

PARAMETER	SEM	P-VALUE	SIGNIFICANCE
BMI-nondiabetics controls	0.940 0.672	<0.00001	HIGHLY SIGNIFICAANT
AIP-nondiabetics controls	0.029 0.052	<0.001	HIGHLY SIGNIFICANT
CRI-1- nondiabetics controls	0.183 0.339	<0.01	SIGNIFICANT
CRI-2 -nondiabetics controls	0.141 0.237	<0.06	NOT SIGNIFICANT
SdLDL - nondiabetics controls	0.425 0.217	<0.0001	SIGNIFICANT

IV. Discussion

Excess fat in visceral adipocytes (central obesity) is root cause of dyslipidemia in obesity. The same is exacerbated by postprandial as well as fasting hypertriglyceridemia which releases free fatty acids into circulation. Tg rich VLDL secreted by liver undergoes hydrolysis by hepatic lipase to form small, dense LDL. The sdLDL are found to be highly atherogenic. Cholesteryl Ester Transfer Protein (CETP) activity is abnormal in both Type 2 DM and Obesity and tends to reduce HDL-C. Thus for a given fasting Tg level, if associated with lowered HDL-C invariably indicates elevation of sdLDL.⁹ Obesity mostly leads to Type 2 DM and associated complications like microvascular changes and atherosclerosis.

In the present study sdLDL was found to be highly significant atherogenic marker both in diabetic and nondiabetic individuals. Though Castelli's risk index 1 and 2 showed variations in different analytical comparisons (Table 2 & Table 6) AIP and sdLDL were constantly on the high end of the scale in both diabetic and nondiabetic obese individuals compared to controls. This correlated with the study of Tan KCB Cooper et al. Gender discrimination could not be established for AIP, CRI-2 and sdLDL in both diabetic obese individuals and nondiabetic obese individuals (p-value <0.515 & <0.24- AIP); (<0.227 & <0.38 - CRI-2) and <0.27 & <0.43 -sdLDL) respectively. These findings did not correlate with those of Eslami et al.¹⁰ Dyslipidemia of obesity adversely affects cardiac functions largely due to elevated LDL-C and reduced HDL-c.

V. Conclusion

Changing life styles, stress and food habits encourage over eating and increase prevalence of obesity more so in urban areas. During routine screening normal expression of lipid profile parameters does not rule out risk of atherogenesis. Risk evaluation can be done by estimation of different ratios and necessary steps can be taken to alleviate the situation. Regular surveillance is required to prevent complications.

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