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Address:-Ashok Yakkaldevi 258/34, Raviwar Peth, Solapur - 413 005 Maharashtra, India
Cell : 9595 359 435, Ph No: 02172372010 Email: ayisrj@yahoo.in Website: www.aygrt.isrj.net

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BODY FAT DISTRIBUTION IN CORONARY ARTERY DISEASE

P. Srilakshmi , M. Vijaya Bhaskar , K. Rambabu , M. F. Gopinath and G. Srinivasa Reddy

Associate Professor , Department of Biochemistry Mamata Medical College and General Hospital Khammam , Andhra Pradesh, INDIA.
Professor and Head , Department of Biochemistry Mamata Medical College and General Hospital Khammam , Andhra Pradesh, INDIA.
Professor of Biochemistry , Mamata Medical College and General Hospital Khammam , Andhra Pradesh, INDIA.
Professor of Cardiology , Mamata General and Super Specialty Hospital Khammam , Andhra Pradesh, INDIA.
Department of Biochemistry ,Mamata Medical College and General Hospital Khammam ,Andhra Pradesh, INDIA.

Abstract:-
BACKGROUND AND OBJECTIVES: Coronary artery disease (CAD) is the leading cause of death and has emerged as major health burden worldwide. The incidence is increasing and is affecting younger age group as well. By 2020, 60% of the world's heart disease is expected to occur in India. The underlying cause of CAD is atherosclerosis. This study of body fat distribution is in terms of blood lipids, body mass index (BMI) and waist circumference (WC).
SUBJECTS AND METHODS: Study group comprised of 145 patients diagnosed as having CAD based on clinical and bio-chemical criteria. Control group included 66 age and sex matched subjects (non CAD cases) using the same criteria.
RESULTS: In this study, significant increase of mean values of serum cholesterol, non-high density lipoprotein cholesterol (Non-HDL–C) BMI, WC and significant decrease in mean high density lipoprotein cholesterol (HDL-C) level were observed in CAD cases when compared with controls.
CONCLUSION: Obesity is markedly observed in CAD cases, cholesterol and Non –HDL- C also increased and HDL –C is decreased.

Keywords: Body fat distribution, CAD, Dyslipedemia, Non-HDL-C .

INTRODUCTION

CAD is the leading cause of death and has emerged as major health burden worldwide[1]. CAD causes 3 million deaths/ year accounting 25% of all mortality in India. 1According to National commission on macroeconomics and health (NCMH) there would be around 62 million patients with CAD by 2015 in India and of these; 23 million would be patients younger than 40 years of age and only 11 million above 60 years of age. By 2020, 60% of the world's heart disease is expected to occur in India. [1]

CAD is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium. The clinical spectrum of CAD is stable angina (SA), unstable angina (UA) and myocardial infarction (MI). [2]

Atherosclerosis is underlying cause of CAD. The pathophysiological origin of this disease depends on the formation and the 'stability' of atherosclerotic plaque. [3] Atherosclerosis is the result of a complex interaction between blood elements, disturbed flow, and vessel wall abnormality; involving several pathological processes: inflammation, with increased endothelial permeability, endothelial activation, monocyte recruitment; growth and proliferation of the smooth muscle cells (SMCs) and lipid accumulation and necrosis. All these processes cumulatively lead to the formation of plaque. [4,5] The major risk factors for atherosclerosis disturb the normal function of vascular endothelium. Hypertension (HTN), smoking, dyslipedemia, insulin resistance (IR), diabetes mellitus (DM) and obesity are commonly recognized risk factors. [6]

The global obesity problem is affecting children, adolescents and adults around the world. By 2015, there will be 2.3

billion overweight adults in the world and more than 700 million of them will be obese. [7] Obesity has reached an epidemic proportion, affecting 5% of Indian population. Indians are genetically more susceptible to weight accumulation in and around the waist. [8] Yusuf et al., [9] reported the prevalence of coronary risk factors in developing countries due to urbanization and considered it as a major coronary risk factor. The causes associated with urbanization of traditional population include decreased physical activity, increased consumption of calorie- rich foods and psychosocial stress. The first two factors lead to increase in weight which causes either generalized (or) central obesity. [10]

Obesity is one of the major health problems worldwide and is strongly associated with increased cardiovascular mortality. [11] Chagas et al., [12] reported greater risk not only related to overweight, but mainly to body fat distribution in the abdominal region with high abdominal fat (central obesity) becoming an important risk factor in the pathogenesis of atherosclerosis in obese patients. Obesity has multiple pathophysiological effects on cardiovascular system. It is a common and important risk factor for many diseases, particularly cardiovascular and metabolic diseases such as diabetes, HTN and dyslipedemia that have deleterious effects on coronary atherosclerosis. [13,14] The importance of abdominal obesity has gained more attention as a component of metabolic syndrome. [15] Weight gain during adolescence should be paid greater attention. [16]

Dyslipedemia refers to the derangement of one or many of the lipoproteins; elevations of total cholesterol, low density lipoprotein cholesterol (LDL-C) and/ TG, or decrease HDL-C. Dyslipedemia may result from over-production or lack of clearance of the lipoprotein particles, or may be related to other defects in the apolipoproteins or metabolic enzyme deficiencies. The altered lipid metabolism in the human body reflects interactions of genetics, complex biochemical processes influenced by medical disorders, medications, and/or environmental factors. Dyslipedemia, particularly hypercholesterolemia and atherogenic dyslipedemia, have been closely implicated in the pathogenesis of CAD. A great deal of attention has been recently given to Asian Indians because of high prevalence of CAD in this ethnic group. Individuals with abnormal fat distribution; appear to be predisposed to developing IR and dyslipedemia. Such a body composition is commonly seen in Asian Indians.

Investigations from several groups, have shown that Asian Indians are predisposed to develop type 2 diabetes, proatherogenic metabolic abnormalities (metabolic syndrome, insulin resistance) and CAD. [17]

MATERIALS AND METHODS:

The study was conducted in the department of biochemistry, Mamata Medical College and General Hospital, Khammam, Andhra Pradesh, India. The patients attending outpatient and wards of cardiology and general medicine departments of Mamata General Hospital and Superspeciality hospital and local cardiac centers were included in this study. Ethical committee clearance is obtained from Institutional Ethical Committee. Informed consent was taken from the participants.

Body fat distribution was assessed by obesity and blood lipids. Obesity was measured by BMI and WC. Body weight, height and WC were measured. BMI was calculated from body weight in kilograms divided by the square of the body height in meters (kg/m2). WC is measured at midpoint between the lower margin of last palpable rib and top of iliac crest. Measurements were taken only for 135 out of 145 cases.Blood lipids analyzed include cholesterol, HDL-C and Non-HDL-C.

Study design:

It was cross-sectional comparative study.Study group comprised of 145 patients diagnosed as having CAD based on clinical and bio-chemical criteria using Electrocardiogaram (ECG) echocardiogram, cardiac biomarkers (myocardial enzymes and troponin) and tread meal test (TMT).

Sex and age matched 66 subjects were recruited as control group (non CAD cases) using the same criteria.5 ml of blood was collected from all the subjects by venipuncture in random condition at the time of presentation at the hospital. Serum was separated within one hour and the parameters were analyzed. Blood lipids analyzed include total cholesterol, HDL-C and Non-HDL-C. Cholesterol was estimated by cholesterol oxidase method, HDL- C by Phosphotungstate precipitation method and measured by colorimeter; where as Non-HDL- C was calculated by subtracting HDL-C from total cholesterol value.

STATISTICAL ANALYSIS

The results were tabulated and analysed using statistical analysis of software (SAS), version 9.3.

Inclusion criteria:

Subjects in the age group of 30-50
Subjects with risk factors DM, HTN and smoking
DM was assessed based on history and WHO criteria
HTN was assessed based on history and JNC-7 criteria
Subjects with normal kidney function

Exclusion criteria

Alcoholics
Subjects with of past history of CAD
Subjects with altered kidney function (random urinary protein > 16 mg/dl and serum creatinine > 1.1 mg/dl)
Subjects on lipid lowering drugs.

RESULTS:

Prevalence of obesity: In our study, the prevalence of obesity has been observed as follows:
Based on BMI, 66 % of cases have shown increased BMI (31 % were overweight and 35 % were obese).
Based on WC, 24 % were normal and 76 % were obese.
Dyslipedemia based on target values:
When the lipid levels were observed in the cases, the following patterns were noted.
72 % of CAD cases had serum cholesterol levels of more than 170 mg/dl (near optimal level for Indians).
When HDL-C level was taken as target, 57 % of CAD cases had < 40 mg/dl.
When Non-HDL-C was calculated with target value of 130 mg/dl, 72 % of CAD cases had more than 130 mg/dl.

DISCUSSION:

The underlying cause of CAD is atherosclerosis and it is rarely fatal alone. It is thrombosis, superimposed on a ruptured or eroded atherosclerotic plaque, which precipitates the life threatening clinical event, ACS. Atherosclerosis is a multifocal, chronic, immunoinflammatory and fibroproliferative disease of large and medium sized arteries fuelled by lipids. Among the multiple cardiovascular risk factors, the number of which is continuously increasing, elevated cholesterol is most unique in being sufficient to drive the development of atherosclerosis. The risk of elevated cholesterol is augmented by lowered HDL and apoA-I lipoprotein which confer protection against atherothrombosis. [18] Hypertriglyceridemia is also a recognized risk factor of CAD. ATP-III guidelines suggested non-HDL-C as a screening test which includes atherogenic lipoproteins, LDL and VLDL. [19]

In our study we observed increased cholesterol, Non-HDL-C and decreased HDL-C in total CAD cases.BMI and WC was also increased in these cases when compared with controls as shown in the Table 1a. The observed, dyslipedemia (cholesterol, Non-HDL-C) correlated with obesity (WC) as shown in the Table 1b.

Majority of CAD cases had serum cholesterol levels more than 170 mg/dl, Non-HDL-C more than 130 mg/dl and HDL-C less than 40 mg/dl as shown in the Table 1c.

Excessive fat accumulation is a consequence of positive energy balance that results from interaction among several factors, including diet (increased intake of energy-dense foods and decreased intake of food rich in micronutrients and bioactive compounds) decreased physical activity (sedentary lifestyle), nutritional and hormonal status in early life as well as genetic, environmental, cultural, and economic factors . [20]

Obesity strongly associated with IR, can result in dyslipedemia. Obesity in general and central obesity in particular enhances the free radical generation that increase oxidative stress which further complicates dyslipedemia, IR and endothelial function. Obesity is common and important risk factor for HTN, DM and MS. HTN, DM and smoking accelerate the disease driven by atherogenic lipoproteins.

One of the possible mechanisms explaining the association between obesity and dyslipedemia is the activation of the AMP-dependent kinase pathway, which is induced by an increase in insulin and leptin, and a reduction in the activation of adiponectin. In obese children, adiponectin is associated positively with insulin sensitivity and HDL-C concentration and negatively with TG concentration. [21]

Lipids are usually measured in fasting state in most of the laboratories in various clinical scenarios. Usually the lipid panel includes total cholesterol, TG, HDL-C and LDL-C. LDL-C is calculated by the Friedwald's formula. LDL-C and HDL-C can also be measured by direct methods, which are costly.

CAD patients are often hospitalized in acute phase. Lipid estimations can pose a problem, if condition of fasting state is adhered. To avoid this problem, random evaluation of lipids (non-fasting lipids) can be useful, which includes total cholesterol, HDL-C and Non-HDL-C.

It was observed that there was not much difference in fasting and non-fasting state for blood sampling to profiles of lipid with exception of TG which are higher in non-fasting state. Unlike LDL-C, which can be incorrectly calculated in the presence of postprandial hypertriglyceridemia, non-HDL-C is reliable when measured in non-fasting state.[22- 24]

Non-HDL-C is obtained from the difference between total cholesterol concentration and HDL-C concentration[25] Non-HDL -C may be calculated on non fasting specimens and may avoid the problem of calculating LDL -C with high TG, essentially making the need for a direct LDL-C assay obsolete. [26]

Non-HDL-C estimation provides information of atherogenic particles including intermediate density lipoprotein cholesterol (IDL-C), VLDL-C, Lipoprotein (a) and LDL-C. Non-HDL-C concept was recommended as secondary target by Third National Cholesterol Education Programme-Adult Treatment Panel (NCEP-ATP-III). [25] Elevated non-HDL -C

signifies increased CVD risk, even if LDL -C levels are at or below the NCEP goal or appear "normal." The importance of Non-HDL-C over LDL -C and TG as a great predictor of CVD was reported in some clinical trials. [24]

CONCLUSION:

CAD is becoming a significant health problem in India. Considering, the increase in the population and the epidemiological transition leading to increase in coronary risk factors, the contribution of India towards CAD death would be much more than that is projected. Many cross sectional studies have clearly demonstrated the association of physical inactivity, obesity, HTN, hypercholesterolemia, hypertriglyceridemia, IR, elevated Lp (a), and low HDL-C with CAD.[6] However, we need prospective cohort studies for evaluation of all coronary risk factors to formulate prevention strategies.

Most of the risk factors may be genetically induced. However, the prospective studies have shown behavioral changes or pharmacological interventions can modify many of them. Hence there is ample scope for prevention of CAD.

The role of lipids and lipoproteins in causation of atherosclerosis is well established since last century. The elevated cholesterol, LDL-C, TG and decreased HDL-C are linked to CAD, directly and indirectly associated with other risk factors. The risk of dyslipedemia becomes more pronounced in CAD in the presence of risk factors like DM, HTN and smoking.

Non-HDL-C has gained attention after NCEP-ATP-III guidelines as secondary target of therapy. When non-HDL cholesterol is used as a target for treatment, more patients would qualify for aggressive drug treatment. [27]

Prevention strategies of CAD can be implemented as follows:

The patients with for patients who already have signs and symptoms of CAD are advised on diet and life style along with pharmacological treatment and interventions.

Identifying individuals with high risk for CAD at an early stage before signs and symptoms appear and provide them with specific diet, lifestyle, and pharmacological advice.

The prevention of onset of risk factors itself beginning with change in social and environmental conditions in which these factors are observed to develop, and continuing for high-risk children, adolescent and young adults. [28]

Evaluation of conventional risk factors like HTN, DM, dyslipedemia and smoking must be done from the younger age itself (third decade onwards).

Estimations of serum lipids must be a part of routine evaluation, which should also include Non-HDL-C.

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Table 1a: Mean ± SD of biochemical parameters of Controls (66) and CAD cases (145).

Parameter	Mean ± SD (Controls)	Mean ± SD (Cases)	t-value	P-value
Cholesterol	162.5 ± 25.9830	201.9 ± 56.8112	5.37	< 0.0001
HDL-C	43.1818 ± 4.7746	39.0138 ± 5.6248	-5.22	< 0.0001
Non-HDL-C	119.3 ± 24.9667	161.9 ± 54.0915	6.10	< 0.0001
Controls (66) versus CAD cases (135)				
BMI	23.3668 ± 3.0605	24.3015 ± 3.1302	2.00	0.0467
WC	87.8939 ± 7.7819	93.1778 ± 8.8080	4.15	< 0.0001

Table 1b: Correlations of biochemical variables in Total CAD cases with r value and p (p* < 0.05, ** < 0.01, * < 0.001, NS: Not significant).**

Variable	Cholesterol	HDL-C	Non-HDL-C	BMI	WC
Cholesterol	1	0.48***	0.98***	-0.04NS	0.25**
HDL-C		1	0.38***	0.06NS	0.15NS
Non-HDL-C			1	-0.04NS	0.26**
BMI				1	0.55***
WC					1

Table 1c: Percentage distribution pattern of lipids, BMI and WC in total CAD cases

	Cholesterol (mg/dl)		HDL-C (mg/dl)		Non-HDL-C (mg/dl)		BMI (Kg/m^2)		WC (cm)	
Group	<170	>170	<40	>40	<130	>130	Normal	Over weight + Obese	Normal	Obese
CAD Total % (145)	27.58 (40)	72.41 (105)	57.24 (83)	42.75 (62)	28.27 (41)	71.72 (104)	34.07 (46)	31.11 (42)	23.7 (32)	76.29 (103)