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NON-HIGH-DENSITY LIPOPROTEIN CHOLESTEROL AND LIPID RATIOS IN THE INCIDENCE OF CARDIOVASCULAR DISEASE IN GERIATRIC POPULATION

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ABSTRACT

Cardiovascular problems have been showing an upward trend in the geriatric population. Management of such problems is a challenging job for physicians. Serum cholesterol is directly correlated with coronary heart disease (CHD) risk. The present study aimed to investigate the correlation between non-high density lipoprotein (non-HDL) cholesterol level, lipid ratios and CHD in the geriatric population. Hundred and five patients were recruited for the study, of which, thirty belongs to control and seventy fifty were test group. Serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol were assayed to measure the level of non-HDL cholesterol and lipid ratios. The differences in non-HDL cholesterol and lipid ratios between groups were compared. The non-HDL cholesterol and lipid ratio level in the geriatric population with CHD group was significantly higher than that in the control group. In conclusion, serum non-HDL cholesterol and lipid ratios were closely associated with development of CHD in geriatric population.

INTRODUCTION

According to World Health Report 2002, cardiovascular diseases (CVDs) will be the largest cause of death and disability by 2020 in India. In 2020 AD, 2.6 million Indians are predicted to die due to coronary heart disease (CHD) which constitutes 54.1 % of all CVD deaths [1]. The National Cholesterol Education Program (NCEP) guidelines for the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults recommend management based on the patient's individual risk of coronary events without providing age-specific treatment guidelines [2].

Globally, as of now, 10 percent of the world population is elderly and it is expected to increase to 21 percent in 2051. Because of this ageing of the population, the incidence and prevalence of CHD are rising significantly. However, estimating the risk of developing CHD is particularly challenging in older persons, as projections based on population studies such as Framingham have not been validated in patients over 75 years of age. The present study aimed to investigate the correlation between non-HDL cholesterol level, lipid ratios and CHD in the geriatric population.

MATERIALS AND METHODS

Patients: The total number of patients included in this study was hundred and five. At the time of admission or entrance all patients responded to a standardized questionnaire covering many personal details (such as smoking habit, alcohol intake, physical activity, food habit, family history, and medical information) organised by trained interviewers. The study population consisted of seventy five patients (test group) with a mean age of 74.7±8.3 years; the control group included thirty patients with mean age of 50.9±6.8 years.

Biochemical parameters and Assay: Samples for the analysis of lipid profile were obtained in the fasting state. The venous blood samples were drawn into pyrogen-free blood collection tubes without additive. The serum was collected after centrifugation at 3500 rpm for 3 minutes and then stored at in a refrigerator until analyzed. Samples were collected from the lab for further analysis. Total cholesterol (TC) and triglycerides (TG) were assayed by routine enzymatic methods using an auto analyser. High-density lipoprotein (HDL) cholesterol was measured using the same enzymatic method after precipitation of the plasma with phosphotungstic acid in the presence of magnesium ions. For cost reasons, low-density lipoprotein (LDL) cholesterol values have long been estimated using the Friedewald formula: [TC] − [total HDL cholesterol] − 20% of the TG value = estimated LDL cholesterol. The VLDL cholesterol is estimated as one-fifth of the TG. The value of TC to HDL cholesterol ratio, TG to HDL cholesterol ratio and LDL to HDL cholesterol ratio were calculated by TC/HDL cholesterol, TG//HDL cholesterol and LDL/HDL cholesterol respectively.

Statistical Analysis: Statistical analysis was performed with SPSS 13 statistical software package. Data were recorded on a pre-designed proforma and managed on spreadsheet. All the

entries were checked for any error. Descriptive statistics for quantitative variables were computed by mean and standard deviation. Means in the two groups were compared by Student's t-test. In this study, $p<0.05$ has been considered as statistically significant.

RESULTS

The study sample in control consisted of 19 males and 11 females and in test group 40 males and 35 females. Table 1 shows the clinical characteristics of the study patients. In test group predominantly male cohort, with a relatively high percentage of smokers, obesity, physical inactivity, hypertension and diabetes when compare with control. Table 2 summaries the baseline mean levels and standard deviation of systolic blood pressure, diastolic blood pressure, sugar and lipid data (TC, TG, HDL cholesterol, LDL cholesterol, VLDL cholesterol, Non-HDL cholesterol, TC/HDL cholesterol, TG/HDL cholesterol and LDL/HDL cholesterol ratio) in the control and test group. There were a significant increase ($p< 0.001$) were found in systolic blood pressure, diastolic blood pressure, sugar, TC, TG, LDL cholesterol, VLDL cholesterol, Non-HDL cholesterol, TC/HDL cholesterol, and LDL/HDL cholesterol ratio in the test group than the control except HDL cholesterol and TG/HDL cholesterol ratio.

Table 1 Clinical characteristics of the study subjects (Non-modifiable and modifiable risk factors)

	Control (n=30)	**Test group (n=75)**
Non-modifiable risk factors		
Age	50.9±6.8	74.7±8.3
Sex M/F	19/11	40/35
Cigarette smoking	8	22
Obesity	3	6
Physical inactivity	4	42
Modifiable risk factor		
Hypertension	5	33
Hypertension (M/F)	3/2	17/16
Diabetes	2	15
Diabetes (M/F)	1/1	9/6
Hypertension + Diabetes /Age >40	1	8
History of Cardiovascular disease	Nil	42

Table 2. Baseline mean level of the biochemical parameters examined in serum samples of all the patients

	Control (n=30)	Test group (n=75)
Non-lipid risk factor /risk markers		
Systolic BP	124.4±12.7	133.3±19.2
Diastolic BP	81.6±9.8	85.6±11.0
Glucose	96.0±17.7	104.6±36.9
Lipid risk factor		
Total cholesterol	137.7±25.1	175.9±23.5
Triglycerides	126.9±31.9	142.6±49.6
High-density lipoprotein cholesterol	36.8±5.2	36.9±6.4
Low-density lipoprotein cholesterol	72.4±25.1	111.6±25.8
Very low-density lipoprotein cholesterol	25.3±6.3	28.5±9.9
Non-high-density lipoprotein cholesterol	101.4±27.4	139.9±23.8
TC/HDL cholesterol ratio	3.8±1.0	4.8±1.0
TG/HDL cholesterol ratio	3.5±1.0	3.9±1.6
LDL/HDL cholesterol ratio	1.9±0.6	3.1±0.9

DISCUSSION

Risk for coronary disease increases steeply with advancing age in men and women. More than half of those who have heart attacks are 65 years or older, and about four out of five who die of such attacks are over the age of 65. At any given level of LDL cholesterol, risk for CHD is higher in the older than in younger people [3]. The principal reason that risk rises with age is that age is a reflection of the progressive accumulation of coronary atherosclerosis, which in turn reflects the cumulative exposure to atherogenic risk factors, both known and unknown. On the average, older persons have more coronary atherosclerosis than do younger persons. Once atherosclerosis develops, the coronary plaque itself becomes a "risk factor" for the development of clinical CHD. This is because plaque ruptures produce acute coronary events (unstable angina or MI), or when plaques grow large, coronary obstructive symptoms (angina pectoris) occur. Recent clinical trials indicate that older persons benefit from LDL cholesterol lowering therapy similarly to middle-aged individuals [4].

Non–HDL cholesterol offers the benefit of being an aggregate measure that includes the concentrations of *all* lipoproteins currently believed to contribute to atherosclerosis. By providing an inclusive measure of all atherogenic particles, there is a strong degree of biologic plausibility for the hypothesis that non–HDL cholesterol is a superior predictor of CVD. Not surprisingly, as TG increase, non–HDL cholesterol correlates with apo B much better than LDL

cholesterol [5, 6]. Several groups encouraged use of non–HDL cholesterol long before supporting longitudinal epidemiologic data was published [7, 8]. The importance of the TG-rich lipoproteins included in the non–HDL cholesterol measure will likely increase as the population ages, becomes more obese, more insulin resistant, and more hyperglycemic [9]. Insulin resistance, which increases with age and obesity, leads to a greater fatty acid flux to the liver with accompanied increased synthesis of VLDL cholesterol.

Data from several population-based cohorts suggests that non–HDL cholesterol is superior to LDL cholesterol for the prediction of cardiovascular events. In 2001, Cui *et al.,* [10] compared the predictive power of non–HDL cholesterol and LDL cholesterol in the 20-year follow-up of the Lipid Research Clinics Program Follow-up Study (LRCPRS). Among 2,406 men and 2,056 women with known coronary disease, there were 234 and 113 cardiovascular related deaths, respectively. Non–HDL cholesterol predicted mortality in both genders, whereas LDL did not show a significant correlation with cardiovascular death in women. A fixed 30 mg/dL increase in non–HDL cholesterol produced a 19% increase in mortality in men and an 11% increase in women, compared to 15% and 8%, respectively, for LDL cholesterol. In 2002, Bittner *et al.,* [11] extended this finding to patients with known CHD undergoing revascularization. Among 1,514 patients enrolled in the Bypass Angioplasty Revascularization Investigation (BARI) trial, non–HDL cholesterol was a significant predictor of both nonfatal MI and angina pectoris, whereas LDL cholesterol and HDL cholesterol did not predict events during follow-up. Lu *et al.,* [12] examined CVD prediction amongst 4,549 patients with diabetes in the Strong Heart Study (SHS).

Finally, two recent studies from the FCS confirm what has been learned about non–HDL cholesterol. First, Liu *et al.,* [13] found that after multivariate adjustment, there was no residual association between LDL cholesterol and risk for CHD after accounting for non–HDL cholesterol, whereas a strong positive and graded association between non–HDL cholesterol and risk for coronary disease after accounting for LDL remained. More recently, Ingelsson *et al.,* [14] reported improved discrimination, better model calibration statistics, and a significant association between non–HDL cholesterol and CHD after adjusting for other risk factors. In their model, the association between LDL cholesterol and CHD was not significant. Non–HDL cholesterol also appears to be a superior predictor of subclinical atherosclerosis.

Lipid parameters can be combined into ratios that reflect the proportion of atherogenic to antiatherogenic lipids and lipoproteins. Proposed lipid ratios for CHD risk assessment include TC to HDL cholesterol, TG to HDL cholesterol, and LDL cholesterol to HDL cholesterol [15, 16, 17]. The ability of the TC to HDL cholesterol ratio to predict development of CHD has been evaluated by statistical tests that compared this ratio with other lipid measures [18]. In a logistic regression analysis, TC to HDL cholesterol was superior to TC alone or LDL cholesterol for identifying individuals at greater risk for subsequent CHD events in 2 general populations (FHS

men and women) as well as a population of high-risk men from the LRC Coronary Primary Prevention Trial (LRC-CPPT). The TC to HDL cholesterol ratio was also superior to LDL cholesterol to HDL cholesterol in the LRC-CPPT cohort, an advantage that may be due to the inclusion of potentially atherogenic VLDL cholesterol (a surrogate for TG) in the numerator of the TC to HDL cholesterol ratio.

A United States case-control study that included 340 patients with no previous history of CHD who were discharged from the hospital after a confirmed MI reported that the TG to HDL cholesterol ratio was a powerful predictor of outcome, possibly because this ratio is so sensitive to the high-risk condition of concomitantly increased TG and decreased HDL cholesterol [17]. The association of TG to HDL cholesterol ratio with CHD risk in the present investigation confirmed previous reports that noted the combination of high TG and low HDL cholesterol (referred to as atherogenic dyslipidemia) [19, 20] to be a powerful risk factor for CHD risk [17, 21, 22]. There is evidence from 1 population study that a high TG to HDL cholesterol ratio might better predict CHD in men than conventional risk factors, such as hypertension, smoking, physical activity [16].

Perhaps the most widely used ratios are LDL cholesterol to HDL cholesterol and TC to HDL cholesterol. Retrospective analysis of the Helsinki Heart Study (HHS) revealed that LDL cholesterol to HDL cholesterol values >5 were associated with increased coronary risk [23], whereas an analysis of 5-year data from the Program on the Surgical Control of the Hyperlipidemias (POSCH) study found that the highest hazard ratios were for LDL cholesterol to HDL cholesterol, with each 1-unit increment associated with a 1.2-fold increase in CHD risk [24]. On the basis of observational data, the TC to HDL cholesterol ratio appears to be a better predictor of subsequent CHD [25]. Data from the FHS indicate that unlike LDL cholesterol, the TC to HDL cholesterol ratio maintains its predictive power in older patients [26], possibly because this measure takes into account TG-rich lipoproteins.

CONCLUSION

In conclusion, serum non-HDL cholesterol level and lipid ratios were closely associated with the development of CHD in the geriatric population. For simplicity, accuracy and reliability non-HDL cholesterol and lipid ratios assessment for CHD risk has a good implication prospect in daily practice.

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