ROLE OF HETEROGENEITY OF LIPIDS IN PREDICTING RISK OF ATHEROMA FORMATION IN METABOLIC SYNDROME

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ABSTRACT

Objective: Assessing impact of heterogeneous lipids in predisposing cardiovascular (CV) atheroma formation in adolescents with metabolic syndrome (MS).

Study Design: Cross-sectional analytical.

Place and Duration of Study: Educational Institutes of Lahore. Six months

Material and Methods: A total of 193, 17-25 year old subjects, 106 males and 87 females were recruited. A record regarding each subject's personal, socioeconomic, educational, dietary and family histories was taken. They underwent the following anthropometric measurements: waist circumference/WC (cm), hip circumference/HC (cm), height (inches), weight (kg), waist hip ratio/WHR, body mass index/BMI and blood pressure. Laboratory investigations included fasting blood samples for glucose and lipids; including total cholesterol (TC), high density lipoprotein-cholesterol (HDL-c), low density lipoprotein-cholesterol (LDL-c) and triglycerides (TG). Calculations for TG/HDL ratio and TC/HDL ratio were made.

Results: Metabolic syndrome (MS) was present in 26 (13.5%) individuals. Male to female ratio was 3:1. Values of waist circumference, blood pressure, fasting plasma glucose, triglyceride and HDL-c, were all high. On comparison of fasting lipid profile, TC/HDL ratio and TG/HDL ratio, it was observed that the average total cholesterol, HDL cholesterol, TCL/HDL ratio were insignificant. The average triglyceride level and TG/HDL ratio were all high. The ROC curve for total cholesterol, HDL-c, TG, TC/HDL and TG/HDL ratio yielded 0.555, 0.526, 0.912, 0.548 and 0.913 areas under the curve. Plasma TG, TG/HDL ratio produced significant *p*-values < 0.001. Abnormal triglycerides and TG/HDL ratio at a cutoff of 3.98 was diagnosed with high sensitivity and specificity.

Conclusion: Fasting triglyceride and HDL-c play a major role in the pathogenesis of MS at an early age. Triglyceride level and TG/HDL ratio as opposed to HDL-c and TC/HDL-c clearly define the risk for development of atheroma formation in our adolescent population.

Keywords: Atheroma, Metabolic syndrome, Triglycerides.

INTRODUCTION

It has been known since decades that increased levels of triglycerides are an independent risk factor for cardiovascular disease. This, combined with deranged levels of other lipid fractions increases the threat even further[1]. Lipid levels are greatly influenced by insulin levels in the body. Resistance of the tissues to this hormone causes worsening of the lipid profile, further leading to heterogeneity of lipid complexes in the plasma, namely increased levels of triglyceride rich lipoproteins (TRL), increased intermediate density lipoproteins and reduced levels of high density lipoproteins[2] (HDL). The metabolism of these various forms of lipids is altered gravely in states of insulin resistance and type 2 diabetes mellitus[3]. Various pro-inflammatory cytokines are elaborated in a number of clinical syndromes; metabolic syndrome is one of them. This syndrome is associated with abnormal expression of enzymes linked with deposition of anomalous forms of lipids[4,5]. The deposition of the abnormal fractions of lipids or atheroma formation in the vascular tree increases risk of atherosclerosis and thrombus formation.

A battery of tests, predict or assess the risk for development of atherosclerotic complications. Fasting lipid profile, C-reactive protein,

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Received: 13 Dec 2012; Accepted: 24 Oct 2013

lipoprotein are few examples[6]. Altered lipid ratios have been implicated as well in predicting the risk of cardiovascular atheroma formation:

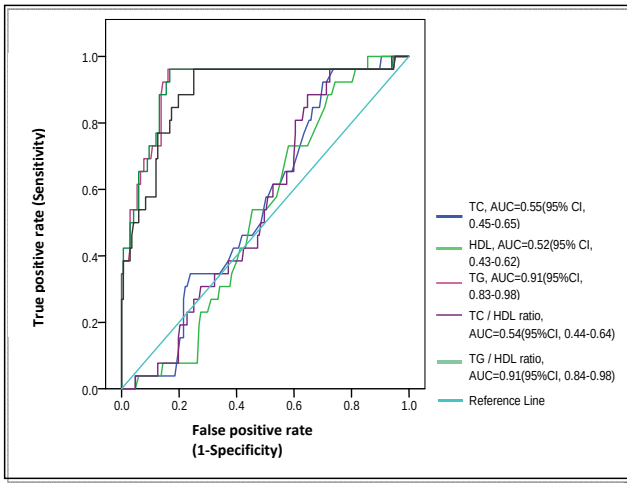

Figure-1: ROC curve of total cholesterol (TC), high density lipoprotein (HDL-c), triglycerides (TG), TCL/HDL ratio, and TG/HDL-c ratio for prediction of atheroma formation in metabolic syndrome.

TC/HDL ratio, LDL/HDL ratio and TG/HDL ratio, are being used for clinical as well as research purposes[7,8]. These ratios show variation depending on gender and ethnicity. Normal cut-off values prevalent in the west may not apply to those residing elsewhere[9,10].

Metabolic syndrome and its various components exist in the adolescent population worldwide[11,12]. In most of these studies, abnormal lipid levels regarding triglycerides and HDL-cholesterol are a common feature. Such profound abnormalities of lipids would eventually lead to earlier onset of cardiovascular outcomes which are the major cause of morbidity and mortality in metabolic syndrome. Recent data in diverse ethnic groups have shown that abnormal lipid ratios are a worthy predictor of such a threat[13]. This study is analysis of how the abnormal lipid profile in such a young age group can help predict outcome to cardiovascular disease (CV) risk. Additionally, an attempt has been made to evaluate the pattern of the lipid fractions prevalent in our younger population.

SUBJECT AND METHODS

A total of 193, 17-25 year old subjects, 106 males and 87 females of middle and upper socioeconomic status were recruited. Individuals diagnosed with maturity onset diabetes of the young, secondary hypertension, type 1 diabetes mellitus and pregnant females were excluded. A record regarding each subject's personal, socioeconomic, educational, dietary and family histories was taken. After written consent, the following anthropometric measurements were done: waist circumference/WC (cm), hip circumference/HC (cm), height (inches), weight (kg), waist hip ratio/WHR, body mass index/BMI and blood pressure. Laboratory investigations included fasting blood samples for glucose and lipids, including total cholesterol (TC), HDL-cholesterol, LDL-cholesterol and triglycerides (TG). TG/HDL ratio and total cholesterol/HDL ratio were calculated.

RESULTS

Analysis for metabolic syndrome according to National Cholesterol Education Program Adult Treatment Panel-III guidelines was done. In this project, 26 (13.5%) individuals met the criteria. Male to female ratio was 3:1. One significant risk factor most prevalent was smoking.

Frequency of abnormal values of waist circumference, blood pressure, fasting plasma glucose, triglyceride and HDL-c, were all significantly higher in cases with MS (Table-1).

When comparison was made for fasting lipid profile, TC/HDL ratio and TG/HDL ratio, it was observed that the average total cholesterol, HDL cholesterol, TC/HDL ratio were insignificant. The average triglyceride level and TG/HDL ratio were all significantly higher in cases with MS (Table-2).

The Receiver Operator Curve for total cholesterol, HDL-c, TG, TC/HDL and TG/HDL ratio yielded 0.555, 0.526, 0.912, 0.548 and 0.913 areas under the curve. Plasma TG, TG/HDL ratio produced significant *p*-values <0.001(Figure-1).

The optimal cut-off decided for triglyceride was 150 mg/dl and diagnosed MS with 92.3% sensitivity and 98.6% specificity. The same sensitivity and specificity was given for TG/HDL ratio at a cutoff of 3.98. Notable positive predictive values of 46.2% each for TG and TG/HDL ratio were observed (Table-3).

Table-1: Distribution of components of metabolic syndrome according to national cholesterol education program adult treatment panel (NCEP ATP III) guidelines.

Components of MS	Metabolic syndrome (n=26)	Control (n=167)	*p*-value
	n (%)	n (%)	
High waist circumference	3 (11.5)	1 (0.6)	0.004
Low HDL-c	26 (110.0)	147 (88)	0.013
High fasting plasma glucose	7 (26.9)	3 (1.8)	<0.001
High triglyceride	24 (92.3)	26 (15.6)	<0.001
High blood pressure	22 (84.6)	45 (26.9)	<0.001

Table-2: Comparisons of lipid and lipid ratios between groups with and without metabolic syndrome.

Fasting lipid profile and lipid ratios	Metabolic syndrome (n=26)	Control (n=167)	*p*- value
	mean ±SD	mean ±SD	
Total cholesterol (mg/dl)	167.12 ± 25.53	165.66 ± 40.40	0.858
HDL cholesterol (mg/dl)	37.13 ± 1.76	37.09 ± 3.64	0.913
Triglycerides (mg/dl)	206.35 ± 63.25	108.88 ± 38.86	<0.001
Total cholesterol/hdl ratio	4.48 ± 0.49	4.44 ± 0.79	0.706
TG/HDL ratio	5.55 ± 1.60	2.95 ± 1.03	<0.001

Table-3: Receiver operator curve characteristics for significant lipid measurements in predicting atheroma formation in metabolic syndrome.

Variables	Cut-off	Sensitivity (%)	Specificity (%)
Total cholesterol (mg/dl)	157	57.7	49.1
HDL cholesterol (mg/dl)	36.5	46.2	50.3
Triglycerides (mg/dl)	150	92.3	83.2
Total cholesterol/HDL ratio	4.32	57.7	49.1
TG/HDL ratio	3.98	92.3	83.2

DISCUSSION

This study suggests the presence of metabolic syndrome in the sample adolescent participants with a frequency of 26%. Sedentary lifestyle, unhealthy eating habits, stress, lack of exercise are major causes of such high prevalence at this young age. These results are in conformity with data in various population studies[14-16] with the syndrome now becoming rifer in earlier years of life.

It is present more so in males as compared to females with a ratio of 3:1. Females though have a greater tendency to develop MS with increasing age[17,18], results of this and various other studies are contrary. These results are valid considering the protective effect of estrogens in the female on lipid profile before menopause[19]. Out of all the risk factors associated with the disease, namely, family history of obesity, type 2 diabetes mellitus, hypertension or myocardial infarction and smoking, the latter showed the highest incidence. Considering smoking is involved in the pathogenesis of atheroma formation[20], its finding as the most prevalent risk factor would

eventually have a grave impact on the outcome of cardiovascular complications.

NCEP ATP III (three) classification has been used to assess the presence of MS in this study. Out of all the components required to classify the presence of the disease, abnormal levels of HDL-c and triglycerides are the most prevalent followed by high normal range of blood pressure. Such are the findings of numerous studies in a younger population[11,15] where the presence of such altered fasting metabolic profile regarding lipids is coming up. This trend emerging in a younger age group needs to be explored further.

Comparison of various lipid fractions among each other reveals our population to have far more deranged levels of TG/HDL-c ratio as compared to TC/ HDL-c ratio. The implication of this ratio alters with ethnicity; various populations all over the world show varied results[21,22]. In our population it is still a valid predictor of cardio metabolic risk.

The ROC curves for fasting lipids and lipid ratios syielded significant areas under the curve. (Figure-1).

The optimal cutoff of 3.98 for triglycerides has been proposed by this study. Though lower levels of 3.4 have been quoted[23], considering influence of race and ethnicity, this point needs further research in our part of the world.

CONCLUSION

High density lipoprotein and triglycerides are deranged in the Pakistani adolescent population along with profoundly altered ratio of TG/HDL-c. TG/HDL ratio is a better indicator of cardiovascular disease risk.

Acknowledgments

I am particularly in debt to the academic support of Dr. Khatoon Akhtar Bano, Director Pakistan Medical and Research Council, Lahore, Pakistan

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