Serum Lipid Profiles and Anthropometric Measurements are Possible Independent Predictor for C3 in Apparently Healthy Kurdish Adults.

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***Abstract*--** **Objectives: To evaluate the association between serum concentrations of complement factor-3 with anthropometric measurements, lipid profile (total cholesterol, triglyceride, high density lipoprotein HDL, low density lipoprotein LDL, very low density lipoprotein VLDL), and lifestyle features in healthy young Kurdish adults.**

Materials and methods: C_3 and ceruloplasmin is determined by Immunoturbidemetric assay, serum lipid profile, blood glucose, uric acid and total protein determined by colorometric methods, body mass index (BMI) measurements were also done.

Results: Significantly positive correlation found in between C3 levels and LDL. Significant differences in means are found in the level of C3 and ceruloplasmin in smokers and non-smokers.

Conclusion: Serum level of LDL may be independent predictor for C3 level and ceruloplasmin and C3 might constitute a risk factor of developing atherosclerosis or cardiovascular disease in smokers.

INTRODUCTION

The complement is a system of proteins connected on a functional level that interact with each other to provide many of the effector functions of humoral immunity and inflammation. The central component of the complement system is the C3 fraction, as all the pathways for activation of the system converge there [1].

Soluble complement components are present in the blood in precursor forms and need to be activated to fulfill their specific physiological roles[2].

Activated complement has diverse functions, including the initiation of inflammation, recruitment of leukocytes, clearance of immune complexes, neutralization of pathogens, regulation of antibody responses, and disruption of cell membranes[2].

Three pathways can activate the complement cascade. The classical activation pathway depends on assembly of complement factors at sites of antigen–antibody complexes. The lectin pathway is initiated by mannan-binding lectin bound to pathogen surfaces. Activation of the alternative pathway is triggered by a variety of pathogen surfaces and requires the interaction of third complement component (C3), factor B (FB), and factor D. Regardless of the pathway, activation leads to the cleavage of C3 [3].

Adipocytes are an important source of C3 production in addition to that produced in the liver in response to interleukin-1 and in activated macrophages. It has been shown that adipose tissue produces all the factors of the alternative pathway for activation of the complement [4].

There is a correlation between C3 levels and the majority of conventional risk factors, in both the general population [5] and in patients with cardiovascular disease and also a positive correlation was found between baseline insulin levels and C3 levels [6].

Concentrations of C3 positively correlate with both visceral and subcutaneous fat [7] and body mass index [7]. Although few studies have been exclusively carried out on a large number of subjects [8].

In addition, an increasing amount of data shows that serum C3 correlates with several metabolic risk factors such as metabolic syndrome [6]

C3-derived peptides have been implicated in the regulation of lipid metabolism. C3a and C3a $_{\text{des-Arg}}$, a peptide formed when the C-terminal arginine is removed from C3a by carboxypeptidase N, can act as acylation-stimulating protein [9]. ASP has been implicated in adipose tissue function and maintenance of metabolic homeostasis [10]. ASP and C3a increase fat storage in adipocytes through increased triglyceride synthesis and decreased intracellular lipolysis [11].

This study is performed to ascertain whether if there is an association between C3 and BMI, and to assess comparatively the relationships of C3, biochemical (lipid profile) and lifestyle features (smokers and alcoholism) in healthy young Kurdish adults.

Subjects and methods

Subjects:

A cross-sectional study was performed on a 50 healthy adult male population of Kurdish origin aged in between 15-60 year. This was according to the questionnaire designed for the study. University of Sulaimani ethical committee approved the study. Informed consent forms were filled out by all of the adults participating in the study.
Any cases with chronic heart disease, chronic renal disease and chronic liver diseases were excluded from the present study.

Blood samples

10 ml of Blood samples after 9-12 hours of fasting were obtained from healthy adults by vein puncture. Samples were allowed to clot at room temperature for 15 min. and then centrifuged at 4000 rpm for 15 minutes.
The serum was aliquoted for making the different determinations on the same day of extraction: glucose [12], total cholesterol and triglyceride([13, 14]) by enzymatic method and high density lipoproteins (HDLs) and low-density lipoprotein by direct method[15-17] in a Cobas C311 automated analyzer. The intra series coefficient of variation was 3.5% for all these determinations. Determination of C 3 level by Immunoturbidemetric assay Human C3c forms a precipitate with a specific antiserum which is determined turbidemetrically [18]
Determination of Blood glucose [12] Uric acid determination[19] protein [20] were also done by Cobas C311.

Anthropometric measures

Blood pressure was measured by a mercury sphygmomanometer to the nearest mmHg, with the subject sitting up, at the end of the visit. Body mass index was obtained dividing body weight by the square of height (kg. m^{*2}). The weight was determined without footwear and with light clothing using electronic scales with an approximation of 0.1kg and a capacity of up to 200kg. The height was measured with a stadiometer with an approximation of 0.5cm.

Statistical analysis:

The data set is analyzed using the Wizard Pro for Mac (Version 1.4.8) by Evan Miller). The significance of differences is to by assessed by ANOVA. In each experiment, correlation study is done with the C3 test by using a Pearson's correlation test. Correlation results is assessed using a 95% Confidence Interval (CI) and a value of $P < 0.05$.

Results:
Significantly positive correlation is found in between C3 with BMI and LDL level figure (1,2) by fisher transformation test $P<0.009$.
Significant differences in means are found in the level of C3 and ceruloplasmin in smokers and non-smokers

Table I
Characteristic features of the study populations according to smoking

Parameters	Non smoker	Smokers	P-value
	Means ±SD	Means ±SD	
Age	43.5±10.7	39.4±10.6	
C_3	145±14.1	113.2±13.1	*
Cholesterol	190±38.1	182.8±36.8	
Triglyceride	183.1±92.9	219.2±111	
HDL	42.0±11.9	37.8±9.6	
LDL	134.8±38.4	124.3±33.3	
VLDL	36.6±18.5	43.8±22.1	
Athrogenic ratio	4.7±1.5	5.0±1.4	
Glucose	96.6±26.7	87.7±7.8	
Uric Acid	5.6±1.3	5.4±1.0	
Protein	6.5±0.8	6.5±0.6	
Ceruloplasmin	25.2±3.7	18.4±2.5	*
BMI	27.1±3.6	26.7±3.1	

Note: * statistically significant differences between the means $P<0.05$.

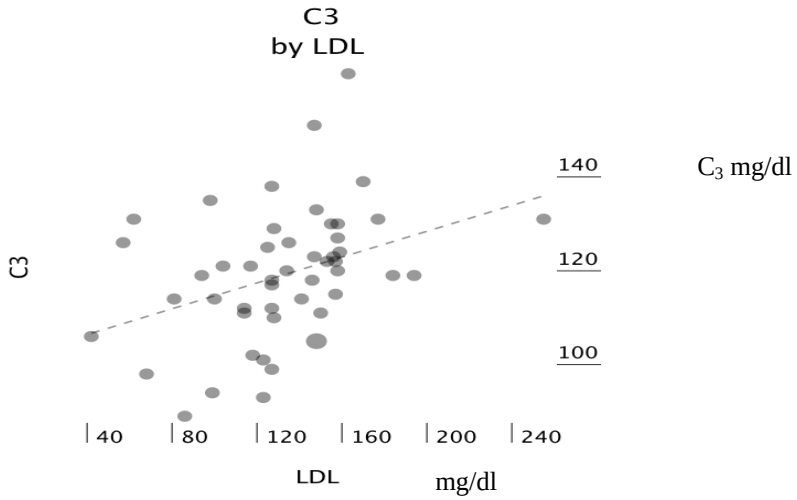

Fig. 1. Significant positive correlation between C3 and LDL.

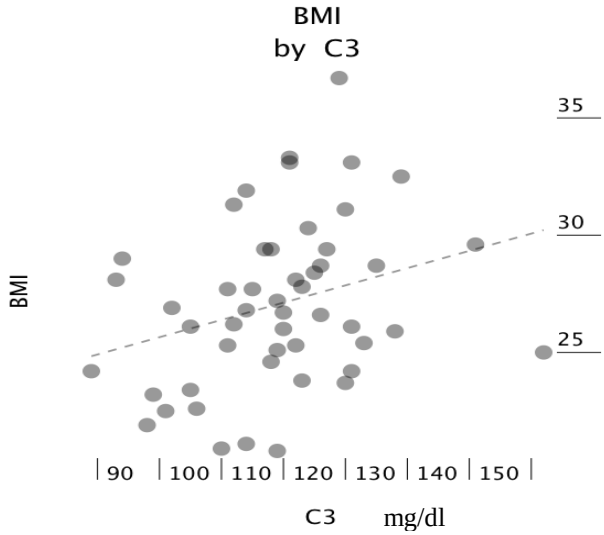

Fig. 2. Significant positive correlation in between C3 and BMI.

DISCUSSIONS

In the present study, the salient finding was that C3 is significantly and positively correlated with the LDL level and BMI. Increased C3 was associated not only with BMI, but also with increased LDL

This might suggest that high concentrations of the acute-phase protein, i.e. ceruloplasmin and C3 might constitute a risk of developing atherosclerosis or cardiovascular disease in smokers. In the present study, there was a change in plasma C3 with increase BMI. Elevated C3 concentrations have been previously reported in adults with obesity, type 2 diabetes, hypertension, hyperlipidemia, and coronary artery disease, all of these known to be associated to obesity [21]. Furthermore, increased C3 has been suggested to be a predictor of myocardial infarction [5], These associations and predictive value of C3 have been reinforced over the last few years, with evaluation of C3 in additional studies as reviewer recently[22] [23]. These associations between lipids, body weight and ASP, even at very early ages, raise the question of what is the signal for increased C3 and its potential role? First, since ASP is generated by adipose tissue, increased adipose tissue mass can lead to increased ASP [22, 24]

In summary, C3 is altered in smokers and high LDL levels. Environmental factors are important risk factor. Furthermore, these changes are associated with modification of lipid profiles, central obesity, and blood pressure, all linked to heart disease that may lead to a chronic state an elderly stage.

Declaration of interest

All authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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