Relation between Types of Age Related Macular Degeneration and Lipid Profile in a Sample of Egyptian Patients

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Abstract

Purpose: To determine whether serum cholesterol level, serum HDL and LDL levels are higher in patients with wet type of age related macular degeneration (ARMD) compared to dry type in a sample of Egyptian patients. To determine whether Cholesterol risk factor is linked more to one type than the other.

Methods: Consecutive non-diabetic cases with ARMD presented to the same physician were included. Patients were divided into two groups, group 1 with Dry AMD, Group 2 with wet AMD. Total Cholesterol (TC) level, Cholesterol ratio, Triglyceride (TAG) level, low density lipoprotein (LDL-C), and high density lipoprotein cholesterol (HDL-C) fasting levels were analyzed and compared.

Results: There was no statistical difference between TC, TAG, LDL-C levels, and cholesterol factor between the two groups. Whereas HDL-C level was shown to be statistically higher in group 2.

Conclusion: High HDL-C level could be a factor enhancing the development of wet type of ARMD in patients with already impaired Bruch’s membrane function rather than developing the dry type. Younger patients with high cholesterol and HDL levels have tendency to develop early advanced wet ARM. Further investigations needed to determine whether controlling blood serum lipids level will result into slower progress of the disease and better response to treatment or not.

Key Words: Age related macular degeneration – Lipid profile – Choroidal neovascular membrane.

Introduction

AGE related macular degeneration (ARMD) is a leading cause of loss of vision, and legal blindness in population over 60 years of age. However few data is available about its incidence or risk factors among Egyptian population. There are two types of ARMD, the dry type which often starts with hard Drusen and ends with geographical atrophy, and the wet type which often starts with soft Drusen and is associated with Choroidal neo-vascular membrane (CNV), exudation and finally macular scar. The pathogenesis is likely multifactorial, involving a complex interaction of metabolic, functional, genetic, and environmental factors, and remains poorly understood [1]. Both types are associated with early impairment of Bruch’s membrane functions and or integrity. The leading pathogenetic theory is that of reduced hydraulic conductivity of Bruch’s membrane [2]. The initial stage of the disease is characterized by the accumulation of lipid-rich deposits under the retinal pigment epithelium (RPE) [3-5]. But whether dry or wet AMD will develop, is unpredictable. Does lipid profile pattern has a role in determining the type of developed ARMD? Up till now, studies evaluating the association between serum lipids and ARMD have been inconsistent [6-13], specially, with quite lacking data about this issue among Egyptian patients. The pattern of lipid profile could be a hypothesized factor contributing to the development of wet ARM. To our knowledge this is one of the early studies comparing lipid serum profile among the two types of ARMD.

Material and Methods

Patients with best corrected spectacle visual loss more than 2 lines due to ARMD were included in the study. All consecutive cases examined by the same physician between March 2009 and August 2011, were included until 2 samples of equal number were obtained. Patients were divided into two groups, Group 1 included dry ARMD cases, Group 2 included wet ARMD cases, with either classic or occult CNV. Clinical diagnosis was confirmed by fundus flourescien angiography (FFA) and Optical Coherence Tomography (OCT).

All patients included in this study were above 50 years old, all were non-diabetics, and none of them were known to be hypercholesterolemic.
Patients who are receiving treatment for hyperlipidemia were excluded.

Patients’ data as age, sex, smoking habit, hypertension and history of cardiac diseases or stroke were recorded.

Five milliliters venous blood was collected from patients after 12 hours fasting immediately transferred to plain tubes. After clotting, the serum was separated by centrifugation. Total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and triglycerides (TAG) were analyzed using an auto-analyzer (Dade Behring Dimension® clinical chemistry system, UK). Concentrations of TC and TAG were determined enzymatically [14]. Concentrations of HDL-C were measured after precipitation of apoB-containing lipoproteins using a dextran sulfate and magnesium chloride solution [15]. Concentrations of low density lipoprotein-Cholesterol (LDL-C) was determined by the Friedewald equation [16].

Hypercholesterolemia was diagnosed as serum cholesterol level of ≥240mg/dl [17].

The serum HDL-C was considered high if value exceeded 60mg/dl [17]. Serum LDL-C level was considered high if value was equal to or exceeds 160mg/dl [17]. Cholesterol ratio was calculated by dividing total cholesterol over serum HDL-C [18]. A ratio greater than 3.5 was considered according to the American Heart Association guidelines as high risk of mordidity [19].

Statistical analysis:
Statistical analysis was carried out using the SPSS® (statistical package for social sciences) Software Version 10. Continuous variables were expressed as mean ± standard deviation. Independent sample t-test to test the significance at the univariate level. A p-value of <0.05 was considered significant.

Results
A Sample of hundred and eight patients was included in the study; with equal number of 54 patients in each group. Mean age of patients in group 1 was 68.1±7.7 (mean±SD), 32 males, 22 females. Mean age in group 2 was 65.5±7.8, including 16 males and 38 female. Females outnumbered males in group 2. In (Group 1), mean serum fasting TC level was 219.7±68.7. Ten cases (18.5%) were considered to have high serum fasting TC level in group 1. In (group 2), mean serum fasting TC level was 239.5±74.6mg/dl. Thirteen cases (24%) were considered to have high TC level. The difference between serum cholesterol levels in the two groups was statistically not significant. (p=0.07).

Mean HDL-C level in (group 1) was 59.9±7.4mg/dl, 19 cases (35%) had HDL level above 60mg/dl. Whereas in (group 2) the mean level was 64.3±8.6mg/dl, 23 (42%) cases had HDL-C level above 60mg/dl. The difference between the two groups was considered statistically significant (p=0.003).

Mean LDL-C level in (group 1) was 122±35.1mg/dl. Six cases (11%) were considered to have high LDL-C level. In (group 2) LDL-C level was 126.8±44.7mg/dl, seven cases (13%) had high LDL-C in (group 2). The difference was statistically non-significant (p=0.2).

The mean Cholesterol risk factor was 3.6±1 in (group 1), 3.7±1.2 in (group 2) the difference was statistically non significant (p=0.3).

In (group 1) , 23 cases (42.5 %) reported history of smoking more than 4 years, while in (group 2) only 9 cases (16.7%) were smokers for more than 4 years duration.

Group 1 included 34 (62.9%) cases known to be hypertensive and are on antihypertensive treatment. Group 2 included 31 (57.4%) cases. None of them were discovered to be hypertensive for the first time during the study.

Patients with history of cardiac insufficiency and/or stroke were higher in group 1 than group 2 [ 16 (29.6%) cases in group 1 versus 4 cases (7.4%) in group 2].

Triglycerides (TAG) serum level in group 1 was 108.2±26.4mg/dl, in group 2 was 115.8±27.4mg/dl, difference was statistically non significant (p=0.07).

It has been noticed by the examiner that younger patients with choroidal neovascularization (CNV) were those with the highest cholesterol level, or HDL-C levels.

Discussion
Previous histological studies showed that cholesterol has been found in Drusen and in Bruch’s membrane [20]. LDL-C and HDL-C cholesterol, vitamin E, lutein and zeaxanthin are present within the retinal pigment epithelium (RPE) and Bruch’s membrane for photoreceptors metabolism. However in older eyes lipoprotein transportation through Bruch’s membrane is not as easy as it was before.
This may result into deposits accumulation and Drusen formation which eventually stresses the RPE, which then may lead to ARMD [20]. The origin of cholesterol found within the retina is uncertain, it could be locally produced or of systemic origin [20]. That is why assessment of the relationship between circulating lipids and the development of which type of ARMD is important. Several studies have evaluated the relationship between ARMD and serum lipids showed inconsistent results [6-13], this could be due to the fact that in previous studies, both types of ARMD were evaluated as one disease.

Previous studies showed that there is a relation between elevated serum cholesterol level and ARMD [10,12,13]. In this study number of patients considered to have high cholesterol level in group one was 18.5%, whereas for group 2, it was 24%, which agrees with previous data. In this study, more patients with higher Cholesterol level were those with wet type ARMD.

Cardiovascular diseases have been linked to ARMD, were some risk factors are believed to overlap as history of smoking and body mass index [21]. Exposure to cigarette smoke or the smoke-related redox molecule, results in the formation of sub-RPE deposits, thickening of Bruch’s membrane, and accumulation of deposits within Bruch’s membrane. Smoke-related oxidants may be another oxidative injury stimulus to the choriocapillaris and RPE, and may explain the association between cigarette smoking and early AMD [22]. Again, no previous clinical studies showed whether it is more linked to either the dry or wet type. In our study smokers with dry type ARM outnumbered those with wet type ARMD, (42.5% vs 16.7%). Although this could be contributed to the higher number of males in group 1, still one laboratory study showed that nicotine reduces vascular endotheliod growth factor (VEGF) secretion and phagocytotic activity in porcine RPE [23].

The present study suggests high levels of HDL-C to be a factor enhancing the development of wet type ARMD. The role of HDL-C in ARMD has been controversial, some studies suggested that patients with high HDL-C level are more prone to develop ARMD [6,8], while other studies suggested high levels of HDL-C to be a protective factor against the development of ARMD in general [12]. On the other hand, a study by Tomany et al., suggested no significant association, either positive or negative between HDL-C and ARMD [9]. Abalain et al. compared 84 patients with ARM with 62 patients of matching age and sex as a control group, they also found no difference in total cholesterol, triglycerides, phospholipids, high- and low-density lipoprotein-cholesterol concentrations between ARMD patients and controls [11].

The relationship between raised blood pressure and ARMD is also non-conclusive. Some studies showed a strong association between higher systolic blood pressure and ARMD [7,24]. Other study showed no correlation [25]. In our study, there was almost the same number of hypertensive patients in both groups.

Identification of factors enhancing the occurrence or progress of ARMD remains cardinal in figuring out ways of preventing the disease, since till now, its pathology is not reversible. Identifying factors in favor of development of one type rather than the other helps better understanding the disease. HDL-C level was statistically significant in wet ARMD group. More patients with history of cardiac disease or stroke were present in group 1, were HDL-C was lower. Smoking was related to the dry type. Further investigations involving more risk factors on larger sample are needed for further documentation of the results. Lipid profile adjustment may contribute to better results with current treatment modalities.

References


