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IS THERE A ROLE OF ESTIMATION OF SERUM LIPID PROFILE LEVEL IN MEIBOMIAN GLAND DYSFUNCTION?

Ophthalmology

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ABSTRACT

Aim: To determine any association between meibomian gland disease and fasting serum lipid profile level.
Setting: Hospital based study
Patients and methods: A case control study of 100 patients (cases) with symptoms and signs of Meibomian gland disease (MGD) and 100 patients (controls) without any symptoms of MGD, between November 2014 to September 2016. Investigations such as Tear film break up time (TBUT), Schirmer's test, fluorescein and rose bengal staining for the eye along with fasting lipid profile was performed for all the patients. Study groups both cases and controls were compared using Chi square test using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA).
Results: Statistically significant elevation of total cholesterol (P=0.00), triglycerides (P=0.00) and LDL levels (P=0.046) were found in MGD cases.
Conclusion: Patients with MGD with no history of hypercholesterolemia may have higher blood cholesterol levels (P=0.00) and triglycerides levels (P=0.00) and LDL levels (P=0.046) than controls of similar age without MGD. If this finding is confirmed by larger studies, MGD may become a marker of previously unknown hypercholesterolemia.

KEYWORDS

Meibomian gland disease, fasting serum lipid profile, eyelids

Introduction

The meibomian glands, named after the German physician Meibom in 1966, are specialized sebaceous glands within the eyelids. Meibomian glands are responsible for secretion of a lipid rich mixture called meibum on to the tear surface through small opening found on the lid margin. Chemical analysis of lipids secreted from normal meibomian glands shows that it consists of a mixture of non-polar lipids (wax esters, cholesterol, and cholesterol esters) and polar lipids (phospholipids and glycolipids).[1] Meibomian gland dysfunction is the most common cause of evaporative dry eye. Left untreated dry eye initially causes irritating ocular surface symptoms and signs that can threaten visual impairment, cause corneal perforation and blindness.[2]

Although the importance of the lipid layer in tear composition is well accepted, but there is little information about whether dyslipidemia resulting from systemic lipid disorder is related to DED (Dry eye disease). Some epidemiologic data have reported conflicting results about such an association. A case – control study concluded that patients with moderate to severe meibomian gland disease (MGD), a major cause of evaporative DED, have a higher incidence of dyslipidemia with respect to elevated TC than the general population. On the other hand, one prospective cohort study showed that although the presence of MGD does not correlate with dyslipidemia, the prevalence of high TG and LDL increases with increasing severity of MGD. [3,4]

At present, there are only a limited number of studies investigating a link between MGD and blood lipids. Current study was done to determine the association between meibomian gland disease and dyslipidemia.

Patients and methods:

Study design: Observational case control study.

Source of data

This was a hospital based clinical study of 100 patients (cases) with symptoms of MGD and 100 patients (controls) without any symptoms of MGD who presented to the department of ophthalmology, between November 2014 to September 2016. After obtaining an ethical clearance from institutional ethics committee, an informed consent was obtained in local language from all the patients included in the study.

Method of data collection:

A detailed history regarding patient name, age, sex, occupation, presenting symptoms, duration and progression were taken. Patients with presenting complaints of burning, irritation, redness, watering or intermittent visual blurring frequently seen in MGD were included as cases in the study whereas patients without clinical features of MGD were grouped under controls. After measuring best corrected visual acuity a detailed slit lamp examination of eyelids was performed using meibomian gland disease classification and grading of lid changes. [5] (Table 1)

Table 1. Slit lamp examination:

Zone	Grading	Feature
Lid margin	thin=1, thick=5	Thickness
	0/1	Rounding
	0/1	Vascularity
	0/1	Hyperkeratinisation
	0/1	Trichiasis
	0/1	Irregularity
	1-3	Mcj
Orifices	0/1	Numerical reduction
	0/1	Capping
	0/3	Pouting
	0/1	Narrowing
Tarsal plate	0/3	Hyperemia
	0/1	Cysts
	0/3	Papillae
	0/3	Follicles
Others	0/3	Concretions
	0/1	Chalazion

Investigations such as Tear film break up time (TBUT), Schirmer's test, fluorescein and rose bengal staining were done in patients. [6-8] Van Bijsterveld scoring system for rose Bengal stain was used to evaluate the intensity of staining based on a scale of 0-3 in 3 areas: nasal conjunctiva, temporal conjunctiva and cornea. With this system, the maximum possible score is 9. According to this system, a score of 3.5 or greater was considered positive for dry eye.[9] Fluorescein staining [10] was graded from 0-3.

0 – no staining of corneal epithelial surface
1 – Mild staining occupying < 1/3 of corneal epithelial surface
2 – Moderate staining occupying < 1/2 of corneal epithelial surface

3 – Severe staining occupying > 1/2 of the corneal epithelial surface.

Systemic hypertension was measured for each patient, it was defined as a systolic blood pressure of >130 mm Hg or a diastolic blood pressure of >90 mm Hg or the current use of systemic antihypertensive drugs. Patients with diabetes are included in the study. Diabetes was defined as a measured fasting blood sugar of >126 mg/dl or current use of anti-diabetic medication.

Patients already on regular topical medications, omega 3 fatty acid drugs, anti – hyperlipidemic drugs were excluded from the study. Patients with history of rheumatoid arthritis and any previous ophthalmic surgery were also excluded from the study. Parameters of dyslipidemia (Total cholesterol > 200mg/dl, low density lipoprotein (LDL)>130mg/dl, High-density lipoprotein (HDL) < 40mg/dl, Triglycerides >150mg/dl and Very low density lipoproteins (VLDL)>30 mg/dl) in MGD patients compared with controls.

FASTING SERUM LIPID PROFILE:

The lipid profile includes total cholesterol, HDL-cholesterol (often called good cholesterol), LDL-cholesterol (often called bad cholesterol), and triglycerides. BECKMAN COULTER 480 analyzer was used for analyzing fasting serum lipid profile. The cut-off value of dyslipidemia was any of the following: hypercholesterolemia (TC ≥ 200 mg/dL); hypertriglyceridemia(TG ≥ 150 mg/dL); low HDL (<40 mg/dL); or high LDL (≥130mg/dL).[11-13]

Data analysis:

The results were statistically analyzed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). Variables including total cholesterol, triglycerides, LDL, HDL, VLDL readings were expressed in Mean ± standard deviation. Study groups both cases and controls were compared using Chi square test, and P value 0.05 or less were considered to indicate a significant difference. Microsoft word and Excel 2007 have been used to generate graphs, tables etc.

Results

200 patients participated in the study of which 100 patients were with symptoms of MGD attended to the department of ophthalmology, ASRAM Hospital, ELURU during the period of September 2014 to October 2016 and 100 patients were without any symptoms of MGD were selected. There were 46 males and 54 females in cases group and 51 males and 49 females in control group. Mean age for cases and controls are 69.6 ± 8 and 65.2 ± 7 respectively. And mean BMI for cases and controls are 27.5 + 4 and 25.7 ± 3 respectively. Diabetes patients in cases and controls are 15% and 16%. Hypertension patients in cases and controls are 18% and 19% respectively. (Table 2)

Table 2. Baseline characteristics of demographic and medical factors of cases and controls.

	Cases	Control
Age (Mean+ SD)	69.6 + 8	65.2 ± 7
BMI (Mean+ SD)	27.5 + 4	25.7 ± 3
Diabetes %	15	16
Hypertension%	18	19

Total cholesterol <200mg/dl was present in 45% of cases and 76% of control >200mg/dl was present in 55% of cases and 24% of controls. It was statistically significant (P=0.00). Triglycerides level <150mg/dl was present in 51% of cases and 27% of controls and >150mg/dl was present in 49% of cases and 73% of controls. It was statistically significant (P=0.00). <40 mg/dl HDL was present in 62% of cases and 38% of controls and >40mg/dl of HDL was present in 67% of cases and 33% 0f controls. It was statistically not significant (p=0.55).<130 mg/dl of LDL values was present in 75% of cases and 25% of controls and >130mg/dl was present in 87% of cases and 13% of controls. It was statistically significant (p=0.046) < 30mg/dl of VLDL was present in 41% of cases and 29% of controls and >30mg/dl was present in 59% of cases and 71% of controls. It was statistically not significant (P=0.103). (Table 3)

Table 3. Lipid profile of cases vs controls

	Cases	Control	p value
Total cholestrol(mg/dl)			
<200	45	76	0.00
>200	55	24	
Triglycerides(mg/dl)			
<150	51	27	0.00
>150	49	73	
HDL(mg/dl)			
<40	62	67	0.55
>40	38	33	
LDL(mg/dl)			
< 130	75	87	0.046
> 130	25	13	
VLDL(mg/dl)			
< 30	41	29	0.103
> 30	59	71	

Discussion

Meibomian gland dysfunction (MGD) is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/ quantitative changes in the glandular secretions altering the tear film leading clinically apparent inflammation and ocular surface disease.[14]

Meibomian gland dysfunction is the most common cause of evaporative dry eye. Left untreated, dry eye initially causes irritating ocular surface symptoms and signs that can threaten visual impairment, cause corneal perforation and blindness. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface, as described in the international DRY EYE WORKSHOP, 2007.[15] Obstructive type meibomian gland dysfunction (MGD), also called meibomianitis, is characterized by the inspissations of meibomian lipids, resulting in a hypo secretion of lipids in tears.[16] The alteration of tear lipid content due to MGD can cause tear film instability, which presents as dry eye symptoms. The melting point of meibum is 30 – 34°C and that of cholesterol is 148°C.[17] The elevated concentration of cholesterol in meibum can elevate its melting point, which theoretically can increase the viscosity of meibum resulting in plugging of the meibomian gland.[18]

One study done by Morozova R.P et al, attempted to associate serum cholesterol and human tear fluid and found that cholesterol concentration in the tear film bore no correlation to serum cholesterol. However, this research measured the concentration of cholesterol in the aggregate tear film. It did not measure this concentration in the lipid layer, in the meibum, or in the meibomian gland. Altered meibomian lipid concentration, including an increase in meibum cholesterol, has been shown to cause dry eye symptoms.[19] Similar study conducted by DAO AH et al, studied the association of dyslipidemia in moderate to severe meibomian gland dysfunction. 66 patients were taken, divided into two groups , one group with moderate to severe MGD others were controls who are followed for one and half year . Patients in cases group had higher incidence of dyslipidemia with respect to elevated total cholesterol (p = 0.0012) when compared to controls. Hence, they concluded that patients with moderate to severe MGD had a higher incidence of dyslipidemia with respect to elevated cholesterol than the general population as reported by data from the National Health and Nutrition Examination Survey.[20] Similar study done by puneet singh braich et al to investigate the relationship between meibomian gland dysfunction and dyslipidemia. Case control study was done, 60 patients with MGD compared to 63 age matched controls from the population. Dyslipidemia was found in 58.3% of cases and 6.3% of controls. Patients in cases group had higher incidence of dyslipidemia with respect to elevated total cholesterol, LDL and HDL levels when compared to controls. All the differences were statistically significant with (p< 0.01).[21] In the present study comparison of the total cholesterol levels in both cases and controls groups were done. However, there was statistically significant elevation of total cholesterol level (p=0.00) was seen in cases group.

Bukhari et al, studied the associations between the grade of meibomian gland dysfunction and dyslipidemia. 132 patients with MGD and 104 without MGD were taken, Patients in cases group had higher incidence of dyslipidemia with respect to elevated triglycerides level (p= 0.002) when compared to controls. Hence, they concluded that patients with severe MGD had a higher incidence of dyslipidemia with respect to elevated triglycerides levels than the controls.[22] Similar study done by Yoon Hong Chun et al total cholesterol and lipoprotein composition are associated with dry eye disease in Korean women. 5627 adults aged above 19 years who were clinically diagnosed with dry eye disease were taken as cases and their blood lipid levels (total cholesterol > 200 mg/dl, triglyceride > 150 mg/dL, low levels of high-density lipoprotein <40 mg/dl, or high levels of low-density lipoprotein >100 mg/dl were analyzed and they were compared with normal population

with no dry eye disease. Results showed that patients with dry eye disease had elevated triglycerides levels with (P value = 0.133). The above study concluded that patients with DED with no previous history of dyslipidemia, Diabetes, Hypertension, have elevated serum triglyceride levels when compared to normal population. [23] In the present study comparison of the Triglycerides levels in both cases and controls groups revealed a statistically significant elevation of triglycerides levels (P value =0.00) were present in MGD cases when compared to controls.

Jasmine Mary Jacob et al conducted a study to determine the association between the presences of meibomian gland dysfunction (MGD) and the individual components of the blood lipid profile in the age group of 40 to 70 years, with complaints of dry eye. Patients were allotted into two group's patients with MGD (cases) and patients without MGD (controls). A fasting lipid profile was done for these groups. HDL levels were compared between both groups. Mean + SD values of cases were 44.3+9.9 and controls were 47.3+14.2 respectively. The above study concluded that there was no statistically significant elevation of HDL levels (P=0.06) between cases and controls.[24] Similar study done by Dao et al their study found that statistically decreased prevalence of patients with low HDL in patients with moderate to severe MGD compared with controls. The cause of this is unknown, but findings suggest that elevated HDL may be a risk factor for the development of meibomian gland disease, despite its cardio protective effects.[20] In the present study there was no statistically significant elevation of HDL levels (P=0.55) In MGD patients when compared to controls.

Mary Jacob et al also studied the association of dyslipidemia with meibomian gland dysfunction. This study also found a correlation between LDL and MGD but there was no significant association between MGD and VLDL. [24] Antonia Pinna, MD et al, conducted a study to investigate a possible correlation between MGD and hypercholesterolemia in young and middle aged patients. 60 symptomatic patients with MGD with no history of hypercholesterolemia and 63 controls without MGD are included in the study, fasting blood lipid level of total cholesterol, LDL, HDL was done. The above study concluded that patients with MGD with no history of hypercholesterolemia may have higher blood cholesterol and LDL levels than controls without MGD.[25] In the present study there was a statistically significant elevation of LDL (P=0.046) was present as compared to VLDL levels (P=0.103) in MGD patients when compared to controls.

Another study done by Roh,Hyun cheol MD et al, systemic comorbidities of dry eye syndrome. This study was done to identify systemic comorbidities in patients with dry eye syndrome. Two years prospective study conducted in patients above 20 years in patients with dry eye disease. Results of this study shows systemic comorbidities like dyslipidemia, arthritis, thyroid disease and renal failure were associated with a significantly higher prevalence of dry eye syndrome.[26]

Similar study was done by Hye won park et al, The association between symptoms of Dry eye syndrome and metabolic outcome in a general population in Korea. They investigated the association between DES symptoms and metabolic syndrome and they taken cases adults aged ≥ 19 years using population-based data from the Korea National Health and Nutrition Examination Survey V. A sample group of 15,294 adults (42.67%men and 57.33% women) completed household interviews in which they analyzed blood lipid levels (for high-density lipoprotein cholesterol, triglyceride, and total cholesterol). However, results of this study shows a significant association between DES and hypertriglyceridemia in women (OR, 1.13; 95% CI, 1.01–1.29). Therefore hypertriglyceridemia might be an important factor in the association between DES and Metabolic syndrome.[27] Further research is needed to evaluate this relationship. Results of the present study shows that patients with symptoms of meibomian gland dysfunction had elevated levels of triglycerides with respect to statistically significant p value (P value =0.00).

The results suggest that patients with MGD with no history of Hypercholesterolemia may have higher blood cholesterol levels (P=0.00) and Triglycerides levels (P=0.00) and LDL levels (P=0.046) than controls of similar age without MGD. If this finding is confirmed by larger studies, MGD may become a marker of previously unknown hypercholesterolemia. Ophthalmologists may increase their role in the early detection of an important risk factor for cardiovascular disease.

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