Egyptian Journal of Clinical Ophthalmology "*EJCO*"
An International peer-reviewed journal published bi-annually
Volume 6, Issue 1, June 2023: pp: 49-56 www. ejco.sohag-univ.edu.eg

Original Article

ASSOCIATION BETWEEN THE LEVELS OF SERUM LIPID AND PRIMARY CLOSED ANGLE GLAUCOMA

Ezz eldawla, M.[1(*)], Sayed, Sh.[2] & Sinjab, A.[1]
[1]Ophthalmology dept., Faculty of Medicine, Sohag, Univ., Egypt. [2]Clinical pathology dept., Faculty of Medicine, Sohag, Univ., Egypt.

[*]*E-mail: mohammedezz44@icloud.com*

Received: 24/2/2023
Accepted: 1/4/2023 **Doi:** 10.21608/ejco.2023.305204

Abstract
Purpose: *to investigate if or whether there is a connection between serum lipid levels and primary angle-closure glaucoma.* ***Patients and methods:*** *This study is prospective and non-randomized. There were 400 participants total, and they were split into two groups. The first group included 200 patients of PACG, and the Second group included 200 patients of a healthy control group of the same age and sex. For measuring serum lipids for all cases, 12hrs fasting-blood samples were collected, and the enzymatic method (autoanalyzer) was used to assess it. The lipid profile includes all of the total cholesterol, triglycerides (TGL), high-density lipoproteins (HDL), and low-density lipoproteins (LDL). According to the guidelines of National Cholesterol Education Program: Adult Treatment Panel III (NCEP: ATP III), the reference values for lipids were taken. Hence, according to which Hypercholesterolemia is defined as total cholesterol greater than 200 mg/dl, Hypertriglyceridemia, when triglycerides greater than 150 mg/dl, LDL greater than> 130 mg/dl were considered high, and HDL less than 40 mg/dl will be considered low.* ***Results:*** *there was a statistical significance at (p-value < 0.01) for triglyceride. On the other hand, the control group had higher levels of HDL, LDL, and cholesterol than the PACG group. Statistically, there was a significant difference for both HDL and LDL levels at p-value <0.01. In addition, the serum CHOL, HDL, and triglyceride levels were positively correlated with the IOP levels in the study group, while the serum LDL was negatively correlated. In the control group, all parameters showed a positive correlation with the IOP level. The correlation was statistically significant only for LDL in the study group and HDL in the control group.* ***Conclusion:*** *The serum triglycerides of PACG patients are noticeably greater than those of the control group. Increased serum HDL, triglyceride, and cholesterol levels are significantly linked with PACG.*

Keywords: *Glaucoma, lipids, triglyceride, Cholesterol*.

1. Introduction
Glaucoma represents a progressive glaucomatous optic neuropathy leading to visual field defect. Many factors cause this pathology, but metabolic conditions, including diabetes mellitus, hypercholesterolemia, and hypertriglyceridemia, can increase glaucoma's pathogenesis [1]. The protocol for PACG diagnosis includes the frequent examination of patients over 60 years at least once a year. But, further examinations must be provided for patients with risk factors [2]. The disorders of lipid metab-

olism can result from the deficient income of lipids food, improper lipid digestion, or cell lipid metabolism disorders [3]. Atherosclerosis genesis is mostly caused by triglycerides and cholesterol. Moreover, the values of serum lipids relate to the age of the patients. They reach the high pick in the thirties, with an end up to the fifth decade for men, but later for females [3]. Total lipids involve phospholipids, triglycerides, and cholesterol. Lipoprotein is transported lipid in the blood categorized into high-density lipoprotein (HDL), very low-density lipoprotein (VLDL), as well as low-density lipoprotein (LDL) [4]. HDLs are cholesterol cleaners, so they are identified as a protective factor in atherosclerosis genesis [5-7]. The present paper aims to detect the correlation between the values of serum lipid, on the one hand, and the incidence, severity, and control of primary angle closure glaucoma, on the other.

2. Patients and Methods

The Ethics Committee of Sohag University approved this study carried out following the Declaration of Helsinki. In addition, all participants in the current study provided an informed consent. Cases with PACG were collected from the Ophthalmology Clinic, Sohag University Hospital, from Abril 2021 to October 2022. Control subjects were collected from individuals attending the Ophthalmology Clinic at Sohag University Hospital during the study period. The study included the medical history for data collection, e.g., body weight, hypertension, and diabetes.

2.1. *Examination*

All participants were examined at Sohag University Hospital, including an ECG, X-ray, and an evaluation of hepatic and renal functions, heart rateas well as blood pressure. Each PACG patient was also examined ophthalmologically. Measuring IOP was performed by the Goldmann applanation tonometer, fundus test was done using an indirect ophthalmoscope, visual field assessment was done using Humphery perimetry (Zeiss, United states), and gonioscopy was done using three mirror Goldmann contact lenses. Laboratory tests were done in the Department of Clinical Pathology, Sohag University Hospital. Blood was sampled in the morning after twelve-hour fasting. For 10 minutes and at 3,000 r/min., the tubes were centrifuged. Enzymatic colorimetry (Riele Photometer 5010, Berlin, Germany) was utilized to measure the serum of HDL, LDL, triglyceride as well as cholesterol levels.

2.2. *Diagnostic and inclusion criteria*

2.2.1. PACG cases

The diagnosis of PACG, according to the criteria, includes narrow anterior chamber angles, glaucomatous optic neuropathy, as well as the VF defect. A cluster of three or more non-edge contiguous points was used to determine the VF defect on the pattern of the deviation plot that did not cross the horizontal meridian. Also, the PACG was diagnosed in eyes with narrow angles, elevated IOP (IOP > 21 mmHg), with 180° of the closed angle at least. The inclusion criteria were the absence of systemic disease in patients above 40 years with a lack of secondary glaucoma or other eye diseases that might impact VF or visual acuity without intraocular surgeries. A total of 240 participants were collected. We excluded 40: neovascular glaucoma {10}, cataract {30} with a final sample of 200 cases: (recently diagnosed PACG cases {70}, and referral PACG cases {130}.

2.2.2. Control subjects

Collecting the normal subjects was from the Ophthalmology Clinic at Sohag Univ. Hospital. Each normal control participant was examined ophthalmologically, including gonioscopy, slit-lamp biomicroscopic, and refractive status. The normal participants' inclusion criteria included individuals above 40 years in the absence of systemic diseases with a lack of any glaucoma or eye diseases that might influence VF or visual

acuity and the lack of any intraocular surgeries. A total of 250 control participants were collected. Later, we excluded 50 (cataract {40}, missed {10} with a final sample of 200 control subjects.

2.3. *Statistical analysis*

STATA v. 14.2 (STATA Statistical Software: Release of 14.2 College Station, TX: StataCorp LP.) was utilized to analyze the data. The Kolmogorov–Smirnoff test helped assess normality. The representtations of quantitative data included the range, median, standard deviation, and mean. Moreover, the student t-test was done to analyze the data to make comparisons between the means of two groups in the case of the normal distribution of the data. In the case of the lack of data's normal distribution, the Mann-Whitney test was utilized. Comparisons were made between categorical data using the chi-square test. The Spearman's correlation coefficient was employed to report correlations between lipid levels and IOP. The analyses of linear regression were adopted to determine the correlation between the levels of lipid and IOP. To determine the risk factors of ACG, logistic regression analyses were carried out. The P-value <0.05 was significant.

3. Results

This study aims to investigate if or whether there is a connection between serum lipid levels and primary angle-closure glaucoma. 200 patients with ACG were included in this study. There were 125 females (62.5%) and 75 males (37.5%). the mean age ± SD was 55.15 ± 5. 200 patients with ACG were included in this study. There were 125 females (62.5%) and 75 males (37.5%). the mean age ± SD was 55.15 ± 5. Table (1) reveals that control participants had considerably greater HDL and LDL levels than the ACG group, while triglycerides were considerably greater in the ACG group than in the control group. Regarding the cholesterol level, it was higher among the control group, but with a non-significant difference. The intraocular pressure was significantly higher among the ACG group than the control subjects (being 26.72 ± mmHg among ACG compared to only 13.55 ±2.61 mmHg among the controls). According to the data shown in this tab. (2), the percentage of patients in the ACG group who had abnormal HDL and triglyceride levels was noticeably greater than that of the control subjects. On the other hand, although the vast majority of ACG and control subjects had abnormal LDL and cholesterol, the differences were non-significant. Table (3) shows that there was a negative, weak, and highly significant correlation between IOP and LDL in the ACG group patients. The association between IOP and triglyceride level, on the other hand, was modest, positive, and significant. The HDL and cholesterol showed non-significant correlations to the IOP. Table (4) shows that there were positive, weak, and significant correlations between IOP and each of the HDL and cholesterol levels in the control group. On the other side, the LDL and triglyceride showed non-significant correlations to the IOP. Table (5) shows that the LDL showed a highly significant and negative linear relation to the IOP in the ACG group, depending on both unadjusted (univariate) and adjusted (multivariate) linear regression analysis. The HDL showed positive linear relation only in the adjusted regression coefficient. Other variables (triglycerides and cholesterol) showed non-significant linear relation to the IOP. Table (6) shows that the HDL showed significant and positive linear relation to the IOP in the control group, depending on both unadjusted (univariate) and adjusted (multivariate) linear regression analysis. Other variables (triglycerides, LDL, and cholesterol) showed non-significant linear relation to the IOP. Table (7) shows that the LDL showed a highly significant inverse relation to the IOP, depending on both unadjusted (univariate) and adjusted (multivariate) logistic regression analysis.

The HDL showed significant inverse relation only in the non-adjusted regression coefficient. Other variables (triglycerides and cholesterol) showed non-significant logistic relation to the IOP.

Table 1: Serum lipids levels and IOP of the ACG and the control groups.

Variable	ACG (N=200)	Control (N=200)	P-value
HDL (mg/dL)			
▪ Mean (SD)	36.55±23.75	43.2±22.21	0.0004
▪ Median (range)	28 (8:100)	40 (10:98)	
LDL (mg/dL)			
▪ Mean (SD)	166.64±73.81	218.74±117.21	0.0001
▪ Median (range)	150 (65:400)	211 (44:533)	
Triglyceride (mg/dL)			
▪ Mean (SD)	216.68±82.13	212.47±80.02	0.0001
▪ Median (range)	211 (99:600)	190 (52:512)	
Cholesterol (mg/dL)			
▪ Mean (SD)	258.02±107.94	270.31±114.06	0.15
▪ Median (range)	255 (100:600)	283.5 (100:522)	
IOP (mm Hg)			
▪ Mean (SD)	26.72±3.02	13.55±2.61	<0.0001
▪ Median (range)	27 (18:39)	13 (8:19)	

Table 2: Serum lipids levels of the ACG and the control groups.

Variable	ACG (N=200)	Control (N=200)	P-value
HDL (mg/dL)			
▪ Normal	84 (42.00%)	108 (54.00%)	0.02
▪ Abnormal	116 (58.00%)	92 (46.00%)	
LDL (mg/dL)			
▪ Normal	48 (24.00%)	54 (27.00%)	0.49
▪ Abnormal	152 (76.00%)	146 (73.00%)	
Triglyceride (mg/dL)			
▪ Normal	88 (44.00%)	110 (55.00%)	0.03
▪ Abnormal	112 (56.00%)	90 (45.00%)	
Cholesterol (mg/dL)			
▪ Normal	72 (36.00%)	80 (40.00%)	0.41
▪ Abnormal	128 (64.00%)	120 (60.00%)	

Table 3: Correlation between IOP and Serum lipids levels in the ACG group

Serum lipids	Correlation coefficient ®	P value
HDL	0.10	0.16
LDL	-0.32	<0.0001
Triglyceride	0.15	0.03
Cholesterol	0.07	0.30

Table 4: Correlation between IOP and serum lipids levels in the control group

Serum lipids	Correlation coefficient (r)	P-value
HDL	0.28	<0.0001
LDL	0.11	0.11
Triglyceride	0.08	0.23
Cholesterol	0.17	0.02

Table 5: Univariate and multivariate linear regression analysis of IOP-serum lipid levels correlation in ACG

Serum lipids	Unadjusted-regression coefficient (95% confidence interval)	P-value	Adjusted-regression coefficient (95% confidence interval)*	P-value
HDL	0.01 (-0.007:0.03)	0.23	0.03 (0.01:0.04)	0.001
LDL	-0.02 (-0.02:-0.01)	<0.0001	-0.02 (-0.03:-0.02)	<0.0001
Triglyceride	0.003 (-0.002:0.008)	0.24	-0.004 (-0.008:0.0008)	0.11
Cholesterol	0.001 (-0.002:0.005)	0.51	0.0003 (-0.003:0.004)	0.85

***** *adjusted to other serum lipid levels (B) beta from regression*

Table 6: Univariate and multivariate linear regression analysis of IOP-serum lipid levels correlation in the control group.

Serum lipids	Unadjusted-regression coefficient (95% confidence interval)	P-value	Adjusted-regression coefficient (95% confidence interval)*	P-value
HDL	0.03 (0.01:0.04)	0.001	0.03 (0.01:0.05)	0.001
LDL	0.001 (-0.002:0.004)	0.71	-0.002 (-0.006:0.001)	0.21
Triglyceride	0.002 (-0.002:0.007)	0.30	0.003 (-0.002:0.007)	0.26
Cholesterol	0.003 (-0.007:0.006)	0.12	0.001 (-0.003:0.004)	0.60

***** *adjusted to other serum lipid levels (B) beta from regression*

Table 7: Univariate and multivariate logistic regression analysis for the correlation of the serum lipid levels-AGG

Serum lipids	Unadjusted OR (95% confidence interval)	P-value	Adjusted OR (95% confidence interval)*	P-value
HDL	0.987 (0.978:0.996)	0.004	0.991 (0.981:1.001)	0.07
LDL	0.994 (0.992:0.997)	<0.0001	0.995 (0.992:0.997)	<0.0001
Triglyceride	1.001 (0.998:1.003)	0.60	0.999 (0.997:1.002)	0.69
Cholesterol	0.999 (0.997:1.001)	0.27	1.001 (0.998:1.002)	0.63

***** *adjusted to other serum lipid levels. (OR) is odds ratio*

4. Discussion

The purpose of this research is to investigate whether or not there is a link that is can be correlated between the presence of PACG and the levels of serum lipids. After the investigation of the key demographic, medical, and lifestyle co-variables, we found that only the serum triglyceride was higher in PACG cases than in the case of the control group. There was a statistical significance at (p-value < 0.01) for triglyceride. On the other hand, the control group had higher levels of HDL, LDL, and cholesterol than the PACG group. A statistically significant difference was found for both HDL and LDL levels at p-value <0.01. In addition, the serum CHOL, HDL, and triglyceride levels related with the IOP levels positively, while the serum LDL negatively correlated. In the control group, all parameters of LDL positively correlated with the IOP level. The correlation was statistically significant only for LDL in the study group, and for HDL in the control group. The findings of our research highlighted that higher serum HDL, cholesterol, and triglyceride are accompanied by a significantly higher risk of PACG. The results agree with previous studies [8,9]. PACG pathogenesis is complicated, containing anatomical and physiological indices [10.11]. Moreover, the dissociation of lipid metabolism is a valuable risk factor for cardiovascular injuries, and is contributed to several eye affections [12]. Prior work indicated that the deterioration of lipid metabolism or dyslipidemia is connected with various cases of adult glaucoma [13]. Edwards et al. [14] stated that endogenous lipid might be included in regulating IOP homeostasis. Moreover, Tang et al. [15] found that triglycerides appeared with high values, denoting one of the independent risk factors of POAG. Furthermore, the literature documented glaucoma-LDL-C correlation [16,17]. Yilmaz et al. [16] indicated the enhancement of triglycerides and cholesterol indices in low-tension glaucoma. Lee et al. [18] showed the correlation of dyslipidemia with POAG's presence and development. Other papers [19-21] also noted substantial differences in the trabecular mesh, aqueous humor types, and lipid concentrations in glaucoma patients and animal models compared to the control group, indicating a relationship between glaucoma and lipid levels. These results agree with the findings of this paper that dyslipidemia correlated with PAGG's severity and occurrence. Until now, the process

by which dyslipidemia enhances the risk of glaucoma onset and progression has not been defined well. Ishikawa et al. [22] reported that the increase in blood viscosity and peripheral venous pressure were associated with high serum lipid levels and declined aqueous outflow. Recently, Wang et al. [12] documented that the lipid metabolic deterioration might alter hemodynamics as well as destruct the aqueous humor outflow, causing the elevation of IOP. Other studies documented that hyperlipidemia might elevate blood viscosity, impairing the aqueous humor circulation pathway and inducing an increase in the intraocular pressure that can produce glaucoma [23,24]. Furthermore, the elevation of serum lipid indices could produce degenerative alterations in ocular blood vessels, inducing an elevation in producing reactive oxygen species and oxidative stress that initiates glaucoma [21]. Kim et al. [25] declared that the enhancement of LDL-C concentrations might elevate blood viscosity, thus impacting the eye's microcirculation and encouraging producing glaucoma. Many authors did not point to the major confounders connected between the levels of lipids and IOP, e.g., BMI, diabetes, or relevant medications, including statins that strongly relate to IOP. In this study, the univariate and multivariate regression analysis illustrated a statistically significant relation between LDL and VLDL levels with IOP in patients with PACG. HDL levels indicated a strong connection with IOP in the controls. Additionally, LDL and VLDL concentrations significantly correlated with the risk of PACG occurrence. This study had some limitations and constraints. Firstly, this research was carried out in the form of a cross-sectional and case-control study. In addition, the capacity to pinpoint the precise mechanism behind the relationship between PACG and serum lipid levels is severely lacking. Thus, we could not accurately infer the causal relation between the PAGG and the serum lipid levels. Secondly, the participants were Egyptians only, limiting the findings' universality. Thirdly, we neglected the lipid-lowering drugs treatment and the way they could impact the findings of the test. Thus, further multicenter prospective studies with larger samples should be conducted.

5. Conclusion

According to the results of our research, the serum triglyceride levels of the PACG were noticeably greater than those of patients who had been assigned to the control group. Higher serum HDL and cholesterol were significantly correlated with PACG.

References

1. Elisaf, M., Kitsos G., Bairaletai E., et al. Metabolic abnormalities in Patients with primary open angle glaucoma. ***Acta Ophthalmol. Scand***. 2001; 72 (2): 129-132.

2. Moses, E., Kitsos G., Bairaktarie E., et al. Lipids abnormalities in patients with primary open angle glaucoma. ***Acta Med. Ophthalmol***. 2003; 54 (2): 164-167.

3. Damji, K. & Feisal, A. Chronic open angle glaucoma. Review for primary care physicians. ***Canadian Family Physicians***, 2005; 51 (9): 1229-1237.

4. Jameson, J., Fauci, A., Kasper, D., et al. ***Harrison's principles of Internal Medicine***, 21th ed., Mc Graw Hill, Medical Pub. Division. 2005.

5. Kovačević S., Jurin A. & Didović-Torbarina A. Dislipidmija u bolesnika sa Primarnim glaukomom otvorenog ugla. ***Abstracts of the 7th Cong. of the Croatian Ophthalmol. Society with Int. Participation***. Ophthalmol. Croatica, 2007; 16 (1): 51.

6. Egorow, W., Bachaldin, I., Sorokin, E. Characteristics of morphological and functional state of erytrocytes in patients

with primary open angle glaucoma with normalized intraocular pressure. ***Vestn. Ophthalmol***. 2001; 117 (2): 5-8.

7. Mc Gwin, M., Mc Neal S., Owsley C., et al. Statins and others cholesterol lowering medications and the presence glaucoma. ***Arch. Ophthalmol***. 2004; 122 (6): 822-826.

8. Newman-Casey, P., Talwar, N., Nan, B., et al. The relationship between components of metabolic syndrome and open-angle glaucoma. ***Ophthalmology***. 2011; 118: 1318-1326.

9. Kim, M., Jeoung, J., Park, K., et al. Metabolic syndrome as a risk factor in normal-tension glaucoma. ***Acta Ophthalmol***. 2014; 92: e637-e643.

10. Jonas, J., Aung, T., Bourne, R. et al. Glaucoma. ***Lancet***. 2017; 390: 2183-2193.

11. Xinghuai, S., Yi, D., Yuhong, C., et al. Primary angle closure glaucoma: What we know and what we don't know. ***Prog Retin Eye Res***. 2017; 57: 26-45.

12. Wang, S., Xu, L., Jonas, J., et al. Dyslipidemia and eye disease in the adult Chinese population: The Beijing Eye Study. ***PLoS ONE***. 2012; doi: 10.1371/journal.pone.0026871

13. Lin, H., Chien, C., Hu, C., et al. Comparison of comorbid conditions between open-angle glaucoma patients and a control cohort: a case-control study. ***Ophthalmology***. 2010; 117: 2088-2095.

14. Edwards, G., Arcuri, J., Wang, H., et al. Endogenous ocular lipids as potential modulators of intraocular pressure. ***J Cell Mol Med***. 2020; 24: 3856-3900.

15. Tang, B., Shao, M., Li, S. Association between blood lipid level and primary open angle glaucoma. ***Chin J Lab Med.*** 2017; 40: 206-211.

16. Yilmaz, N., Coban, D., Bayindir, A., et al. Higher serum lipids and oxidative stress in patients with normal tension glaucoma, but not pseudoexfoliative glaucoma. ***Bosn J Basic Med Sci***. 2016; 16: 21-27.

17. Modrzejewska, M., Grzesiak, W., Zaborski, D, et al. The role of lipid dysregulation and vascular risk factors in Glaucomatous retrobulbar circulation. ***Bosn J Basic Med Sci***. 2015; 15: 50-56.

18. Lee, S., Kim, G., Lee, W., et al.. Vascular and metabolic comorbidities in open-angle glaucoma with low- and high-teen intraocular pressure: A cross-sectional study from South Korea. ***Acta Ophthalmol***. 2017; 95: e564- e574.

19. Mayordomo-Febrer, A., Lopez-Murciam, M., Morales-Tatay, J., et al. Metabolomics of the aqueous humor in the rat glaucoma model induced by a series of intracamerular sodium hyaluronate injection***. Exp Eye Res***. 2015; 131: 84-92.

20. Aribindi, K., Guerray, Y., Lee R., et al. Comparative phospholipid profiles of control and glaucomatous human trabecular meshwork. Invest ***Ophthalmol Vis Sci***. 2013; 54: 3037-3044.

21. Aribindi, K., Guerra, Y., Piqueras, M., et al. Cholesterol and glycosphingo lipids of human trabecular and glaucomatous donors. ***Curr Eye Res***. 2013; 38: 1017-1026.

22. Ishikawa, M., Sawada, Y., Sato, N., et al. Risk factors for primary openangle glaucoma in Japanese subjects atending community health screenings. ***Clin Ophthalmol***. 2011; 5: 1531-1537.

23. Tan, G., Wong, T. **&** Fong, C. Singapore Malay eye study. Diabetes, metabolic abnormalities, and glaucoma. ***Arch Ophthalmol***. 2009; 127: 1354-1361.

24. Kim,Y., Jung, S., Nam, G., et al. High intraocular pressure is associated with cardiometabolic risk factors in South Korean men: Korean National Health and Nutrition Examination Survey, 2008-2010. ***Eye (Lond)***. 2014; 28: 672-679.

25. Kim, M., Kim, H., Kim, H., et al. Risk factors for open-single glaucoma with normal baseline intraocular pressure in a young population: The Korea Nation Health and nutrition Examination Survey. ***Clin Exp Ophthalmol***. 2014; 42: 825-832.