

Research Paper

IS THERE ANY ASSOCIATION BETWEEN SERUM LIPIDS AND DIABETIC RETINOPATHY IN TYPE 2 DIABETIC PATIENTS IN GHANA?

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ABSTRACT

Aim: To evaluate the association between serum lipids and diabetic retinopathy (DR) in type 2 diabetic subjects.

Study Design: Cross-sectional observational study

Place and Duration of Study: Diabetes and Ophthalmology units of the Komfo Anokye Teaching Hospital, Kumasi in Northern Ghana, between September 2011 and June 2012.

Methodology: Serum levels of total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were assessed in 251 type 2 diabetic mellitus patients. Diagnosis and classification of diabetic retinopathy was based on dilated ophthalmoscopy. Classification of lipid abnormalities was done according to the National Cholesterol Education Programme-Adult Treatment Panel 111 (NCEP-ATP111) Guidelines.

Results: Among 251 type 2 diabetic mellitus patients, 41.0% had retinopathy of which 31% were of the non-proliferative type and 10% were proliferative. The mean $\pm$ SD age of the diabetics with retinopathy was 52.64 ± 11.80 years; their mean duration of diabetes was 17.69 ± 4.06 years. Subjects with DR were older ($P < .001$), had longer duration of diabetes ($P < .001$) and higher fasting blood glucose ($P < .001$) than those without. HDL-C level ($P = .016$) was lower, and TC ($P < .001$), TG ($P < .001$) and LDL-C levels ($P < .001$) were higher in subjects with diabetic retinopathy (DR) compared with those without diabetic retinopathy (NDR). Multiple logistic regression analysis revealed that unadjusted TC (odds ratio [OR] 3.57 [95% CI 4.471-12.26] $P < .001$), TG (odds ratio [OR] 2.25 [95% CI 1.54-3.2] $P < 0.0001$), HDL-C (odds ratio [OR] .664 [95% CI 0.471- 0.938] $P < .001$), and LDL-C (odds ratio [OR] 2.97 [95% CI 2.22-3.96] $P < .001$) were associated with DR. After adjusting for age and duration of diabetes, only TC (odds ratio [OR] 4.00 [95% CI 1.12-14.25], $P = .032$) maintained a significant association with DR. However, after adjusting for fasting blood glucose (FBG), the association of TC with DR lost its significance ($P = .37$).

Conclusion: This study suggests that there is no significant association between serum lipids with DR in Ghanaians patients with Type 2 diabetes mellitus. However, further studies are needed to confirm this finding

Keywords: *serum lipids, diabetic retinopathy, proliferative retinopathy, dyslipidemia, Ghana.*

1. INTRODUCTION

Over 135 million individuals are affected with diabetes mellitus across the world.¹ The prevalence reported for Ghana in the early 1990 s was 2%.² Subsequent studies by Amoah et al. indicated that the prevalence rate rose from 0.4% in the 1950 s to 6.3% in the year 2000 with an average of about 700 new cases diagnosed yearly.³ Diabetic retinopathy is the most common specific complication of type 2 diabetes, resulting in blindness for over 10,000 people with diabetes per year, worldwide.⁴

There is controversy regarding the role of serum lipids in the pathogenesis of diabetic retinopathy.⁵⁻¹¹ Data from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complication Study (DCCT/EDIC) cohort showed that severity of retinopathy is positively associated with serum triglycerides (TG) and negatively associated with HDL-C.⁵ Likewise the Chennai Urban Rural

Epidemiology Eye Study (CURES) showed a statistically significant association between TG and DR.⁶ In contrast, other multi-population studies have not consistently shown similar associations.⁸⁻¹⁰ Ethnic differences might account for variations in result, and accordingly, the difference in allele frequency of lipoprotein phenotypes have been reported to be associated with retinopathy in previous studies.^{12, 13} These differences have also been attributed in part to racial/ethnic differences in diabetes duration, glycemic control, and blood pressure levels.^{14, 15} In contrast to whites, not much is known about the role of serum lipids and lipoproteins in the pathogenesis of diabetic retinopathy in black Africans where diabetic retinopathy is highly prevalent.^{14, 15} Such knowledge is important in developing primary preventive strategies for managing diabetes mellitus related microvascular complications. The purpose of this study was to evaluate the associations of traditional serum lipids and lipoproteins with diabetic retinopathy in type 2 diabetic patients attending an Ophthalmology clinic of a large, urban, managed care hospital in the Ashanti Region of Ghana.

2. MATERIAL AND METHODS

This cross-sectional observational study was carried out at the Komfo Anokye Teaching Hospital in the Ashanti Region of Ghana between September 2011 and June 2012. The center is one of the tertiary health institutions provided by the government of Ghana to serve as a referral center for peripheral health institutions in the country. We consecutively recruited 251 type 2 diabetics who were attending and being followed-up at the diabetes and ophthalmology units of the hospital. The Institutional Ethics Committee of the University of Cape Coast and Komfo Anokye Teaching Hospital approved the study and informed consent was obtained from all study participants.

2.1 Patient evaluation

Patients evaluated at the center had a standardized ocular health assessment which included, slit lamp biomicroscopic examination of anterior segment, direct and indirect ophthalmoscopy for fundus evaluation and tonometry. In addition all participants underwent a standardized health examination and an interviewer administered questionnaire was used to ascertain past medical history, current smoking status, and the use of antihypertensive medications, lipid lowering medications, and oral hypoglycemic agents. Anthropometric measurements including weight and height were obtained. The BMI was

calculated using the formula, weight (kg)/ height (m²). Obesity was defined as BMI > 30 kg/m². The blood pressure was recorded in the right arm while seated. Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or reporting antihypertensive medication use. Classification of lipid abnormalities was done according to the National Cholesterol Education Programme-Adult Treatment Panel 111 (NCEP-ATP111) Guidelines.¹⁶

2.2 Criteria for Exclusion

- Patients who have had an episode of diabetic ketoacidosis, thyroid or liver disease, non-diabetic renal disease, pregnancy, acute or chronic inflammatory syndrome, alcoholism or malnutrition, were not included in the study
- Patients on diuretics, beta-blockers, hypolipemic agents, or any other drug or hormone known to influence lipid or lipoprotein metabolism, were not included.

2.3 Assessment of diabetic retinopathy

The diagnostic criteria for the presence of retinopathy as defined by the Early Treatment Diabetic Retinopathy Study¹⁷ were based on the presence of any of the following characteristic: microaneurysms (MAs), hemorrhages, cotton wool spots (CWSs), intraretinal microvascular abnormalities (IRMAs), hard exudates (HEs), venous beading, and new vessels. Severity of retinopathy was further categorized as proliferative and non-proliferative based on the presence and absence of new vessels proliferating in the optic disc or elsewhere in the retinal background respectively.

2.4 Laboratory Procedures

Fasting blood samples were collected from subjects for biochemical analysis at Laboratory of the Komfo Anokye Teaching hospital, Kumasi. Biochemical analysis of blood samples was performed according to methods described in literature.^{6, 11} TC and TG were determined using the enzymatic method, HDL-C was determined using the precipitation method. LDL-C was determined from the Freidwald's formula: LDL-C = TC- HDL-C - (TG/5). FBG was determined using the glucose oxidase enzymatic method.

2.5 Data analysis

Analyses of data were performed using the SPSS statistical package (Version 16, SPSS Inc, Chicago, IL, USA). The results are expressed as mean± standard deviation (SD). Participants characteristics with and

without DR were compared using a chi-square test for proportions. One-way ANOVA (with *post hoc* Tukey analysis) or unpaired *t*-test, as appropriate, was used to compare groups for continuous variables. Normality was checked, and data was transformed as appropriate. Person data on the basis of the worse eye was used for analysis. Multivariate logistic regression was used to assess the association between serum lipids and DR. Initially, adjustments was made for age, then duration of diabetes and in addition FBS. A $P < 0.05$ was considered significant.

3. RESULTS AND DISCUSSION

Of the 251 diabetic subjects recruited, 41% had retinopathy of which 31% were of the non-proliferative type and 10% were proliferative. The characteristics of the study population according to retinopathy status are shown in Table 1. The age range of all the subjects was 19 to 72 years. The mean $\pm$ standard deviation of age, duration of diabetes and FBG for subjects with diabetic retinopathy was respectively 52.64 ± 11.80 (range 26 to 72), 17.69 ± 4.06 (range 10 to 26 years) and 21.42 ± 2.62 (range 13.10 to 28.20). Subjects with DR were older ($P < .001$), had longer duration of diabetes ($P < .001$) and higher FBG levels ($P < .001$) compared to those without DR. Their BMI was similar. Stratification of these results by gender showed that our findings were similar ($P = .26$) for the women and men (Data not shown). Table 2 shows the prevalence of diabetic retinopathy in the different sub-groups in relation to age, gender, duration of diabetes and other clinical and socio-demographic characteristics. Prevalence of retinopathy significantly increased with increase in age (<40 years, 14.5%; 40-59 years, 78.6%; ≥ 60 years, 100% [$P < .001$]) and duration of diabetes (<5 years, 1.1%; 6-10 years, 3.3%; 11 years and above, 100% [$P < .001$]). There was no significant difference in the prevalence of DR between the hypertensives and the normotensives ($P = .42$). The prevalence of retinopathy was significantly lower ($P = .04$) in those who had attained tertiary education compared to those who hadn't. Table 3, presents the serum lipid levels in the grades of DR compared with those without DR. The HDL-C level ($P = .017$) was lower, and TC ($P < .001$), TG ($P < .001$) and LDL-C ($P < .001$) were significantly higher in subjects with diabetic retinopathy compared to those without diabetic retinopathy. Table 4 shows the data of the retinopathy groups, classified according to the severity of the retinopathy as either proliferative (PDR) or non-proliferative diabetic retinopathy (NPDR). Comparing the levels of

serum lipids in the retinopathy subgroups, it was observed that HDL-C level was lower ($P=.016$), while TC ($P<.001$), TG ($P<0.001$) and LDL-C ($P<.001$) levels were significantly higher in subjects with PDR.

Table 5 shows the profile of lipid abnormalities in diabetics with and without retinopathy according to the National Cholesterol Education Programme-Adult Treatment Panel 111 (NCEP-ATP111) Guidelines. The prevalence of hypercholesterolemia was significantly higher ($P=.01$) in diabetics with retinopathy (62.3%) compared to those without retinopathy (38%). The prevalence of hypertriglyceridemia in diabetics with and without retinopathy was 41.3% and 58.7% respectively, and this difference was statistically significant ($P=.022$).

The results of the regression analysis are presented in Tables 6 and 7. The analysis revealed that only TC ($P<.001$) and LDL-C ($P=.001$) contributed significantly to the predictive ability of the model after adjusting for age. On introducing duration of diabetes into the original model (Table 7), the association of LDL-C with DR lost its significance ($P=0.41$) whereas TC still showed a significant association with DR ($P=.032$), but when FBG was introduced into the model, the association of TC with DR lost its significance ($P=0.368$).

Table 1. Characteristics of the study population according to retinopathy status

Variables	Without Retinopathy	With retinopathy		P-value
		NPDR (n=78)	PDR (n=25)	
Mean Age (years)	29.03±6.9	49.63±11.2	62.40±8.2	.00
Age range (years)	19-57	26-71	42-72	
Gender M:F	40:108	37: 41	8:17	.26
Body mass index (kg/m ²)	22.9±14.83	21.11±2.66	22.37±2.28	.24
Mean duration of diabetes	5.19±2.27	16.53±3.34	21.32±4.04	.00
Duration range	2-10	4-25	17-36	
Mean Fasting blood glucose	10.30±2.27	13.69±2.33	17.96±1.33	.00

Values are expressed as n (%)

Table 2. Prevalence of Diabetic retinopathy in different groups

Variables	Without retinopathy (n=148)	With Retinopathy NPDR (n=78) PDR (n=25)	
Age (years)			
< 40 (n=159)	136 (85)	23(14.5%)	0 (0%)
< 40-59 (n=56)	12 (21.4)	36 (64.3)	8 (14.3)
≥ 60 (n=36)	0 (0)	19 (52.8)	17 (47.2)
Gender			
Males (n=85)	40 (47.1)	37 (43.5)	8 (9.4)
Females (n=166)	108 (65.1)	41 (24.7)	17 (10.2)
Duration of diabetes (years)			
< 5 (n=90)	89 (99)	1 (1.1)	0 (0)
6-10 (n=61)	59 (96.7)	2 (3.3)	0 (0)
11-15 (n=25)	0 (0)	25 (100)	0 (0)
>15 (n=75)	0 (0)	50 (66.7)	25 (33.3)
Hypertension			
Normotensive (n=170)	118 (69%)	48 (28%)	4 (2.3%)
Hypertensive (n=81)	30 (37%)	30 (37%)	21 (26%)
Level of education			
Primary (n=60)	37 (61.7)	17 (28.3)	6 (10)
Secondary (n=105)	56 (53.3)	41 (39.0)	8 (7.6)
Tertiary (n=28)	23 (82.1)	2 (7.1)	3 (10.7)
None (n=58)	32 (55.1)	18 (31.0)	8 (13.8)
Social status			
Employed (n=80)	50 (62.5)	24 (30.0)	6 (7.5)
Self employed (n=69)	26 (37.7)	31 (45)	12 (17.4)
Unemployed (n= 102)	72 (70.6)	23 (22.5)	7 (6.9)

Values presented as no (%)

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168 **Table 3: Mean values of the lipid sub-fractions in subjects with and without retinopathy**

169 Lipid parameters	Without retinopathy	With retinopathy	P-value
170	(n=148)	(n=103)	
Total cholesterol (mmol/l)	4.99±1.10	6.92±0.93	.000
Triglycerides (mmol/l)	1.34±0.71	1.83±0.89	.000
HDL-cholesterol (mmol/l)	1.57±0.81	1.34±0.70	.016
LDL-cholesterol (mmol/l)	3.037±1.25	4.84±1.35	.000
VLDL-cholesterol (mmol/l)	0.92±0.67	0.43±0.57	.451

171 The values are mean ± SD

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173 **Table 4. Mean values of the lipid sub-fractions in subjects categorized according to**
 174 **severity of diabetic retinopathy**

175 Lipid parameters	Non-proliferative retinopathy	Proliferative retinopathy	P-value
176	(n=78)	(n=25)	
Total cholesterol (mmol/l)	6.57 ± 0.07	7.99 ± 0.17	0.000
Triglycerides (mmol/l)	1.67 ± 0.86	2.32 ± 0.11	0.000
HDL-cholesterol (mmol/l)	1.56 ± 1.0	1.30 ± 0.16	0.017
LDL-cholesterol (mmol/l)	4.38±0.15	5.24 ± 0.22	0.000

177 The values are mean ± SD

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Table 5: Profile of lipid abnormalities in sub-groups according to the National Cholesterol Education Programme-Adult Treatment Panel 111 (NCEP-ATP111) Guidelines

Lipid Profile	Without retinopathy (n=148)	With retinopathy NPDR (n=78)	PDR (n=25)
Total cholesterol (mmol/l)			
Desirable < 5.2 (n=89)	87 (97.8)	2 (2.2)	0 (0)
Borderline 5.2 – 6.2 (n=46)	42 (91.3)	4 (8.7)	0 (0)
High risk ≥ 6.3 (n=116)	19 (16.4)	72 (62)	25(21.6)
Triglycerides (mmol/l)			
Normal<1.7 (n=176)	117 (66.5)	49 (27.8)	10 (5.7)
Borderline high risk 1.7-2.3 (n=45)	22 (48.9)	16 (35.5)	7 (15.5)
High risk 2.4-5.6 (n=30)	9 (30)	13 (43.3)	8 (26.7)
Very high risk ≥ 5.7 (n=0)	0 (0)	0 (0)	0 (0)
HDL-cholesterol (mmol/l)			
Men higher risk < 1.03 (n=76)	43 (56.6)	22 (28.9)	11(14.5)
Women higher risk < 1.3 (n=111)	61 (55)	37 (33.3)	13 (11.7)
Men normal 1.03-1.3 (n=25)	18 (72)	5 (20)	2 (8.0)
Women normal 1.3-1.6 (n=16)	8 (50)	6 (37.5)	2 (12.5)
All sexes protected ≥1.6 (n=108)	63 (58.3)	35 (32.4)	10 (9.3)
LDL-cholesterol (mmol/l)			
Optimal value<2.6 (n=56)	51(91%)	5 (9%)	0 (0%)
Optimal value near 2.6-3.3 (n=44)	41(93%)	3 (7%)	0 (0%)
Borderline high risk 3.4-4.1 (n=58)	38 (65.5%)	18 (31%)	2(3.4%)
High risk 4.2-4.9 (n=43)	18(41.9%)	24(55.8%)	1(2.3%)
Very high risk ≥ 5.0 (n=45)	6 (13%)	18 (40%)	21(47%)

Values are expressed as n (%)

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188 **Table 6. Association of serum-lipids with diabetic retinopathy**

Lipid Parameters	B	S.E.	Wald	Sig.	OR	95% CI	
						Lower	Upper
Total Cholesterol							
Unadjusted	2.002	0.257	60.501	0.000	7.405	4.471	12.263
Adjusted for age	1.274	0.275	21.470	0.000	3.576	2.086	6.130
Adjusted for age & duration	1.387	0.648	4.576	0.032	4.002	1.123	14.257
Adjusted for age, duration & FBS	3.425	3.808	0.809	0.368	30.734	0.018	53.680
Triglycerides							
Unadjusted	0.812	0.192	17.886	0.000	2.253	1.546	3.282
Adjusted for age	0.122	0.277	0.193	0.660	1.130	0.656	1.946
Adjusted for age & duration	0.266	1.294	0.042	0.837	1.305	0.103	16.465
Adjusted for age, duration & FBS	1.321	1.732	0.581	0.446	3.745	0.126	111.645
HDL-cholesterol							
Unadjusted	-0.409	0.176	5.408	0.020	0.664	0.471	0.938
Adjusted for age	-0.474	0.303	2.446	0.118	0.622	0.344	1.128
Adjusted for age & duration	0.715	0.959	0.555	0.456	2.042	0.312	13.396
Adjusted for age, duration & FBS	2.185	2.145	1.038	0.308	8.892	0.133	595.311
LDL-cholesterol							
Unadjusted	1.089	0.147	54.852	0.000	2.970	2.227	13.960
Adjusted for age	0.594	0.187	10.111	0.001	1.811	1.256	2.613
Adjusted for age & duration	0.482	0.584	0.680	0.410	1.620	0.515	5.087
Adjusted for age, duration & FBS	0.160	1.266	0.016	0.899	1.173	0.098	14.020

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190 DISCUSSION

191 In view of the controversy regarding the role of lipids in the pathogenesis of diabetic retinopathy, lipid and
 192 lipoprotein levels were estimated in patients with and without retinopathy to assess the association of
 193 these parameters with diabetic retinopathy. Most studies designed to examine this relationship have
 194 revealed conflicting results.^{5,-7,8-10} The reasons responsible for such discrepancies have not been
 195 completely explored, but assumed in part to be due to heterogeneity in subject selection with variable
 196 inclusion criteria, such as age range, gender, diabetic duration, and differences in the methodology and
 197 classification of diabetic retinopathy.⁶

198 In the present study, serum lipids were not associated with retinopathy after adjustment for traditional risk
 199 factors. This finding is compatible with previous studies from the Multi-Ethnic Study of Atherosclerosis

(MESA)¹⁰ which showed no association between serum lipids, including total cholesterol, low density lipoprotein cholesterol, and high density lipoprotein cholesterol and diabetic retinopathy. There are speculations that serum lipids may have a strong influence only in the severe forms of diabetes retinopathy end point.¹¹ This hypothesis is biologically plausible given that serum lipids have been found to be associated with diabetic macula edema (DME) but not with diabetic retinopathy in several studies.^{6, 7, 11} This finding provides additional insight to support the suggestion that serum lipids are involved in the pathogenesis of DME, but not DR, only via exudation of lipids through damaged retinal vasculature, which occurs at a later stage, but may not cause direct injury to the endothelium and consequent damage to the blood retina, which occur at an earlier stage.¹¹ Consistent with this hypothesis, a previous study found that there was no association between serum lipids and development of retinopathy in non-diabetics, indicating the importance of existing damage in retinal vasculature for lipids to exhibit their harmful effect on the retina.¹⁸ Nevertheless, further studies are needed in this area.

Studies of DR have consistently shown age, gender, BMI, duration of diabetes and fasting blood glucose to be independent risk factors for retinopathy.^{8, 9} In this study, there was no association between gender and BMI with retinopathy. As observed in other studies^{6, 7}, the diabetics with retinopathy were older, had longer duration of diabetes and higher fasting blood sugar than those without retinopathy. Some studies carried out on type 2 diabetic patients found no association of lipids and lipoproteins with DR after adjusting for traditional risk factors.^{8, 11} On the contrary other authors reported that some lipid measures are consistently associated with diabetic retinopathy, and this relationship was found to be unaffected by age, gender, duration of diabetes and fasting blood sugar.^{6, 7} In the Chennai Urban Rural Epidemiology Eye Study (CURES), Rema *et al*⁶ reported a significant association of TC with DR after adjustment for age and duration of diabetes which was lost after adjustment for fasting blood sugar. This is consistent with our findings but with slight variation. In our study, the significant association of TC with DR was found to be unaffected by age and duration of diabetes, but on adjusting for FBG, the association disappears, suggesting that the relationship was mediated through glycemic control. A consistent association of poor glycemic control with diabetic retinopathy has been described in a previous study.¹⁹ It may seem feasible to attribute the slight variation in results to variations in subjects' age range and duration of disease across these studies. In our study, mean age of the diabetic subjects with retinopathy was 52.64±11.80

years and their mean duration of diabetes was 17.69 ± 4.06 years. In CURES, the mean age and duration of type 2 diabetics with retinopathy was 53 ± 10 years and 8.0 ± 6.0 years respectively. In the study by Sasongko et al⁷, mean age and duration of diabetes was 62.0 years and 18 years respectively. Sasongko et al included both type 1 and type 2 diabetes mellitus patients in their study. Nevertheless, it remains uncertain to what extent this difference might be explained by variable inclusion criteria in subject selection, such as age range, gender, diabetic duration and FBG.

About 10% of the cases of retinopathy in this study had PDR. This is of great concern given that PDR is vision threatening and its detection is an implication of low frequency of eye exam. It is recommended that people with diabetes should have their eyes examined every 1 to 2 years. Because of the relatively small sample size of PDR subjects, no distinction could be made between NPDR and PDR in the primary analysis.

In comparison with the study of Sasongko et al which was carried out on 224 subjects, this study utilized a slightly larger population (251 subjects). However, there are some inherent limitations. First, the cross-sectional design did not allow for speculation about causality as this would require a prospective follow-up study. Second, diabetic retinopathy diagnosis was based on ophthalmoscopic findings by an Ophthalmologist, rather than the stereoscopic color fundus photography used in large trials such as the Early Treatment Diabetic Retinopathy Study (ETDRS) group.¹⁷ The sensitivity of ophthalmoscopy for the detection of retinopathy has been reported to be 65% as compared to a higher sensitivity of 89% for the seven field retinal photography.²⁰ It is possible that individuals with mild levels of DR may have been missed, thus, the likelihood of underestimating DR proportions in this study sample. However, since we did not find any association between lipids and DR, performing seven-field retinal photography or misclassification of cases is unlikely to have affected our findings. Third, there is a possibility of selection bias that may limit generalizability of our results due to the fact that the subjects were taken from one hospital cohort. However, during the recruitment process, it was realized from the patients' records that they come from all regions of Ghana, given that the center is a major tertiary referral center which serves the nation. Therefore, a selection bias in this regard was unlikely to occur.

254 Despite these potential limitations, our sample was typical of that of other diabetic populations with DR,
255 showing strong associations with age, duration of diabetes and FBG.

256 257 **4. CONCLUSION**

258 This study has demonstrated that serum lipids and lipoproteins may not be associated with DR in
259 Ghanaian diabetics. However further studies are needed to confirm these findings.

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264 265 **COMPETING INTERESTS**

No competing interests exist.

266 **AUTHORS' CONTRIBUTIONS**

267 Dr Ilechie Alex, a Senior lecturer at the Department of optometry, University of Cape Coast
268 (UCC) and Adinortey Micheal, a consultant Biochemist and Senior lecturer at the Department of
269 Biochemistry, UCC, designed the overall study and wrote the protocol and first draft of the
270 manuscript. Lartey S, a consultant ophthalmologist at the Ear, Nose and Throat Department of
271 Komfo Anokye Teaching Hospital and Owusu-Manehene Frank, a Doctor of optometry research
272 student of UCC conducted the recruitment and ocular health assessment of the subjects, and
273 managed the analyses of the study alongside with Dr Ilechie Alex. Amponsah Irene performed
274 the statistical analysis while Boadi-Kusi Berth, Kyei Samuel and Ocansey Stephen, all lecturers
275 at the Department of optometry, UCC, managed the literature searches and were also involved
276 in the original design of the study. Okoh Chuks, a medical scientist based in the US, supplied
277 the materials for clinical assessment and managed the Biochemical analyses. All authors read
278 and approved the final manuscript

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