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Is there any Association between Serum Lipids and Diabetic Retinopathy in Type 2 Diabetic Patients in Ghana?

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Authors' contributions

Authors IAA and MBA designed the overall study and wrote the protocol and first draft of the manuscript. Authors SL and FOB conducted the recruitment and ocular health assessment of the subjects and managed the analyses of the study alongside with IAA. Author IA performed the statistical analysis while authors EKA, SBBK, SK and SO all lecturers at the Department of optometry, UCC, managed the literature searches and also involved in the conception and original design of the study. Author CO a medical scientist based in the US supplied the materials for clinical assessment and managed the Biochemical analyses. All authors read and approved the final manuscript.

Original Research Article

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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 the Ashanti Region of Ghana, between September 2011 and June 2012.

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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 ± 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<0.001), had longer duration of diabetes (P<0.001) and higher fasting blood glucose (P<0.001) than those without DR. HDL-C level (P=0.016) was lower, and TC (P<0.001), TG (P<0.001) and LDL-C levels (P<0.001) were higher in subjects with diabetic retinopathy (DR) compared with those without diabetic retinopathy. Multiple logistic regression analysis revealed that unadjusted TC (odds ratio [OR] 3.57 [95% CI 4.471-12.26] P<0.001), TG (odds ratio [OR] 2.25 [95% CI 1.54-3.2] P<0.0001), HDL-C (odds ratio [OR] 0.664 [95% CI 0 .471- 0.938] P=0.020), and LDL-C (odds ratio [OR] 2.97 [95% CI 2.22-3.96] P<0.001) 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=0.032) maintained a significant association with DR. However, after adjusting for fasting blood glucose (FBG), the association of TC (odds ratio [OR] 30.73 [95% CI 0.018-53.68] P=0.36) with DR lost its significance.
Conclusion: Our analyses suggest 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 1990s was 2% [2]. Subsequent studies by Amoah et al. indicated that the prevalence rate rose from 0.4% in the 1950s 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. MATERIALS 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 diabetic patients 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 (m^2) [6]. The ausculatory method of BP measurement was used as described in literature [16] The BP 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 [16] Classification of lipid abnormalities was done according to the National Cholesterol Education Programme-Adult Treatment Panel 111 (NCEP-ATP111) Guidelines [17]

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.
- Patients who had high intra-ocular pressures (IOP) and could not tell the medications they were using were suspected to be on beta-blockers and were excluded from the study.

2.3 Assessment of Diabetic Retinopathy

Diabetic patients were those diagnosed by physician diagnosis based on the American Diabetes Association and World Health Organization (ADA/WHO) recommended criteria [18]. The diagnostic criteria for the presence of retinopathy as defined by the Early Treatment Diabetic Retinopathy Study [19] 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. Multivariate logistic regression was used to assess the association between serum lipids and DR. Initially, adjustments were made for age, then duration of diabetes and in addition FBG. A $P<0.05$ was considered significant.

3. RESULTS

A total of 251 diabetic patients who fulfilled the inclusion criteria were included in the primary analysis. There were 85 males and 166 females, with an age range of 19 to 72 years. Diabetic retinopathy was present in 103 (41%) patients, with NPDR in 78 (31%) and PDR in 25 (10%). One hundred and forty eight patients (59%) had no retinopathy. The characteristics of the study population according to retinopathy status are shown in Table 1. The mean ± standard deviation of age (years), duration of diabetes, and FBG (mmol/l), for subjects with diabetic retinopathy was respectively 52.64±11.80 (range 26 to 72 years), 17.69±4.06 (range 10 to 26 years), and 21.42±2.62 (range 13.10 to 28.20). The mean ± standard deviation of age, duration of diabetes, and FBG, for subjects without diabetic retinopathy was respectively 29.03±6.9 (range 19 to 57), 5.19±2.27 (range 2 to 10 years), and 10.30±2.27 (range 5 to 15 mmol/l). Subjects with DR were older ($P<0.001$), had longer duration of diabetes ($P<0.001$) and higher FBG level ($P<0.001$) compared with those without DR. BMI ($P=0.24$) was similar in both groups.

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% [$P<0.001$]) and duration of diabetes (<5 years, 1.1%; 6-10 years, 3.3%; 11 years and above, 100% [$P<0.001$]), but not gender ($P=0.26$), hypertensive status ($P=0.42$), social class and level of education ($P=0.12$). Severity of retinopathy significantly increased with increase in age and duration of diabetes

(both *P*<0.001) but not gender, hypertensive status, social class or level of education (*P*>0.05).

Table 1. Characteristics of 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	0.00
Age range (years)	19-57	26-71	42-72	
Gender M:F	40:108	37: 41	8:17	0.26
Body mass index (kg/m^2)	22.9±14.83	21.11±2.66	22.37±2.28	0.24
Mean duration of diabetes	5.19±2.27	16.53±3.34	21.32±4.04	0.00
Duration range	2-10	4-25	17-36	
Mean Fasting blood glucose	10.30±2.27	13.69±2.33	17.96±1.33	0.00

Values are expressed as n (%); NPDR, Non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy

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 (85.0)	23(14.5)	0 (0.0)
<40-59 (n=56)	12 (21.4)	36 (64.3)	8 (14.3)
≥60 (n=36)	0 (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 (0.0)
6-10 (n=61)	59 (96.7)	2 (3.3)	0 (0.0)
11-15 (n=25)	0 (0.0)	25 (100)	0 (0.0)
>15 (n=75)	0 (0.0)	50 (66.7)	25 (33.3)
Hypertension			
Normotensive (n=170)	118 (69.0)	48 (28.0)	4 (2.3.0)
Hypertensive (n=81)	30 (37.0)	30 (37.0)	21 (26.0)
Level of education			
Primary (n=60)	37 (61.7)	17 (28.3)	6 (10.0)
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 (45.0)	12 (17.4)
Unemployed (n= 102)	72 (70.6)	23 (22.5)	7 (6.9)

*Values presented as no (%); Linear trend for prevalence and severity of retinopathy, *One-way ANOVA P < 0.05; NPDR, Non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy*

Table 3, presents the mean ± standard deviation values of the lipid sub-fractions in subjects with and without retinopathy. There was a significant difference in mean levels of HDL-C, TC, TG and LDL-C between the two groups. TC levels were significantly higher in subjects with DR compared with subjects without DR (P<0.001). TG levels were significantly higher in subjects with DR compared with subjects without DR (P<0.001). LDL-C levels were significantly higher in subjects with DR compared with subjects without DR (P<0.001). HDL-C levels were lower in subjects with DR compared to subjects without DR (*P*=0.016). Mean levels of VLDL-C was not significantly different in the two groups (*P*=0.451).

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

Lipid parameters	Without retinopathy (n=148)	With retinopathy (n=103)	*P*-value
Total cholesterol (mmol/l)	4.99±1.10	6.92±0.93	0.000
Triglycerides (mmol/l)	1.34±0.71	1.83±0.89	0.000
HDL-cholesterol (mmol/l)	1.57±0.81	1.34±0.70	0.016
LDL-cholesterol (mmol/l)	3.03±1.25	4.84±1.35	0.000
VLDL-cholesterol (mmol/l)	0.92±0.67	0.43±0.57	0.145

The values are mean ± SD

Table 4 presents data of lipid and lipoprotein levels according to the severity of retinopathy classified as either proliferative (PDR) or non-proliferative diabetic retinopathy (NPDR). Similar to the findings regarding mean lipid levels between subjects with and without DR, there was a significant difference in lipid and lipoprotein levels with the severity of DR. TC levels were significantly higher in subjects with PDR compared with subjects with NPDR (P<0.001). TG levels were significantly higher in subjects with PDR compared with subjects with NPDR (P<0.001). LDL-C levels were significantly higher in subjects with PDR compared with subjects with NPDR (P<0.001). HDL-C levels were lower in subjects with PDR compared to subjects with NPDR (*P*=0.017).

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

Lipid parameters	NPDR (n=78)	PDR (n=25)	*P*-value
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

The values are mean ± SD; NPDR, Non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy

Table 5 shows the profile of lipid levels in diabetics with and without retinopathy according to the National Cholesterol Education Programme-Adult Treatment Panel 111 (NCEP-ATP111) Guidelines. The prevalence of retinopathy significantly increased with increasing levels of TC (<5.2 (desirable) 2.2%; 5.2-6.2 (borderline), 8.7%; ≥ 6.3 (high risk), 83.6%). The prevalence of retinopathy significantly increased with increasing levels of TG (<1.7 (normal) 33.5%; 1.7-2.3 (borderline), 51%; 2.4-5.6 (high risk) 70%). The prevalence of retinopathy significantly increased with increasing levels of LDL-C (<2.6-3.3 (normal), 16%; 3.4-4.1

(borderline) 34.4%; ≥ 5.0 (high risk), 47%). On the other hand, the combined prevalence (men and women) of retinopathy significantly increased with decreasing levels of HDL-C (1.03-1.6 (normal), 78%; <1.3 (higher risk), 88%).

With regards to severity of retinopathy, a similar trend was observed. Severity of retinopathy significantly increased with increasing levels of TC (<5.2, 0%; 5.2-6.2, 0%; ≥ 6.3, 21.6%), TG (<1.7, 5.7%; 1.7-2.3, 15.5%; 2.4-5.6, 26.7%), and LDL-C (<2.6-3.3, 0%; 3.4-4.1, 3.4%; ≥ 5.0, 47%). Severity of retinopathy significantly increased with decreasing levels of HDL-C (1.03-1.6, 20.5%; <1.3, 26.2%).

Table 5. Profile of lipid levels 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 (62.0)	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 (30.0)	13 (43.3)	8 (26.7)
Very high risk ≥ 5.7 (n=0)	0 (0.0)	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 (55.0)	37 (33.3)	13 (11.7)
Men normal 1.03-1.3 (n=25)	18 (72.0)	5 (20.0)	2 (8.0)
Women normal 1.3-1.6 (n=16)	8 (50.0)	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(91.0)	5 (9.0)	0 (0.0)
Optimal value near 2.6-3.3 (n=44)	41(93.0)	3 (7.0)	0 (0.0)
Borderline high risk 3.4-4.1 (n=58)	38 (65.5)	18 (31.0)	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 (13.0)	18 (40.0)	21(47.0)

*Values are expressed as n (%); Linear trend for prevalence and severity of retinopathy, *One-way ANOVA P < 0.05; ** unpaired t-test P<0.05; NPDR, Non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy*

Table 6 presents the results of the regression analysis using DR as the dependent variable. Before adjustments for all covariables, the analysis revealed that unadjusted TC (odds ratio [OR] 7.40 [95% CI 4.47-12.26] *P*<0.001), unadjusted TG (odds ratio [OR] 2.25 [95% CI 1.54-3.28] *P*<0.0001), unadjusted HDL-C (odds ratio [OR] 0.66 [95% CI 0 .47- 0.93] *P*=0.020), and unadjusted LDL-C (odds ratio [OR] 2.97 [95% CI 2.22-13.96] *P*<0.001) were associated with DR. After adjustment for age, only TC (odds ratio [OR] 3.57 [95% CI 2.08-6.13] *P*<0.001) and LDL (odds ratio [OR] 1.81 [95% CI 1.25-2.61] *P*=0.001) were associated with DR. When duration of diabetes was introduced into the original model, the association of LDL-C (odds ratio [OR] 1.62 [95% CI 0.51-5.08] *P*=0.41) with DR lost its significance

whereas TC (odds ratio [OR] 4.00 [95% CI 1.12-14.25] *P*=0.032) maintained a significant association with DR. However, on introducing FBG into the model, the association of TC with DR lost its significance (odds ratio [OR] 30.73 [95% CI 0.018-53.68] *P*=0.36).

Table 6. Association of serum-lipids with diabetic retinopathy

Lipid Parameters	Sig.	OR	95% CI	
			Lower	Upper
Total Cholesterol				
Unadjusted	0.000	7.405	4.471	12.263
Adjusted for age	0.000	3.576	2.086	6.130
Adjusted for age & duration	0.032	4.002	1.123	14.257
Adjusted for age, duration & FBG	0.368	30.734	0.018	53.680
Triglycerides				
Unadjusted	0.000	2.253	1.546	3.282
Adjusted for age	0.660	1.130	0.656	1.946
Adjusted for age & duration	0.837	1.305	0.103	16.465
Adjusted for age, duration & FBG	0.446	3.745	0.126	111.645
HDL-cholesterol				
Unadjusted	0.020	0.664	0.471	0.938
Adjusted for age	0.118	0.622	0.344	1.128
Adjusted for age & duration	0.456	2.042	0.312	13.396
Adjusted for age, duration & FBG	0.308	8.892	0.133	595.311
LDL-cholesterol				
Unadjusted	0.000	2.970	2.227	13.960
Adjusted for age	0.001	1.811	1.256	2.613
Adjusted for age & duration	0.410	1.620	0.515	5.087
Adjusted for age, duration & FBG	0.899	1.173	0.098	14.020

4. DISCUSSION

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

In the present study, serum lipids were not associated with retinopathy after adjustment for traditional risk 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 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 diabetic macula edema but not diabetic retinopathy, 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-diabetic patients, indicating the importance of existing damage in retinal vasculature for lipids to exhibit their harmful effect on the retina [19]. Nevertheless, further studies which should include patients with diabetic macula edema is suggested in Ghana.

Studies of diabetic retinopathy have consistently shown age, gender, body mass index, 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 body mass index with retinopathy. As observed in other studies [6,7], the diabetic patients 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 diabetic retinopathy 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 total Cholesterol with diabetic retinopathy 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 total Cholesterol with diabetic retinopathy 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. Consistent associations of poor glycemic control with diabetic retinopathy has been described in previous studies [20,21]. 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 diabetic patients with retinopathy was 53±10 years and 8.0±6.0 years respectively. In the study by Sasongko et al. [7], mean age and duration of diabetes was 62.0 years and 18 years respectively although 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.

A similar trend was observed regarding the association between serum lipids and severity of diabetic retinopathy. High density lipoprotein cholesterol levels were lower and total Cholesterol, triglycerides and low density lipoprotein cholesterol levels were higher in subjects with proliferative diabetic retinopathy compared with subjects with non-proliferative diabetic retinopathy. The detection of cases of proliferative diabetic retinopathy in this study is of great concern given that PDR is vision threatening and its detection is an implication of low frequency of eye exam among the people. It is recommended that people with diabetes should have their eyes examined every 1 to 2 years.

Previous studies usually focused only on the association of lipid levels with the presence of retinopathy without performing a more complete analysis of characteristics of lipid profiles in subjects with retinopathy. In our study a significant proportion of diabetic subjects with retinopathy have high risk lipid levels. In light of the clinical implications for the management of serum lipids and lipoprotein levels in patients with diabetic retinopathy, such as decreasing risk of hard exudates formation and preservation of visual acuity [6,7,11] our results highlights the need to improve health education among diabetic patients in Ghana.

In comparison with the study of Sasongko et al. [7] which was carried out on 224 subjects, this study utilized a slightly larger population (251subjects). 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 [19]. The sensitivity of ophthalmoscopy for the detection of retinopathy has been reported to be 65% as compared to a higher sensitivity of 89% for seven field retinal photography [21]. 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. Despite these potential limitations, our sample was typical of that of other diabetic populations with DR, showing strong associations with age, duration of diabetes and FBG.

5. CONCLUSION

Our analyses suggest that diabetic retinopathy in Ghanaians is not associated with serum lipids and lipoproteins levels. However, in light of the results of various studies, management of serum lipids and lipoprotein levels in patients with diabetic retinopathy have other important clinical implications such as decreasing risk of hard exudates formation and preservation of visual acuity. Large population studies are needed in Ghana to confirm our findings.

CONSENT

All authors declare that 'written informed consent' was obtained from the patients who comprise the study sample, and authorities of the Komfo Anokye Teaching Hospital for publication of this report.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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