Original Article

Comparison of Ocular Biomery in Primary Open Angle Glaucoma and Non-glaucoma in South West Nigeria

Abstract

Background: Glaucoma is a public health problem in Nigeria. The number of individuals affected by glaucoma in Nigeria is much higher than the individuals known to have the disease. Ocular parameters such as intraocular pressure, central cornea thickness, axial length and refractive error have all been documented as risk factors of glaucoma especially among Caucasians and African Americans, with little documentation in Africa where there's an alarming rate of blindness. **Aim and Objectives:** To compare central cornea thickness (CCT), intraocular pressure (IOP), axial length (AL) and refractive state in participants with primary open angle glaucoma (POAG) and non-glaucoma in South-West Nigeria. **Materials and Methods:** This hospital-based case-control study was carried out among 184 newly diagnosed POAG and non-glaucoma adult participants attending the outpatient clinic of Eleta eye institute. The CCT, IOP, AL and refractive state were measured in each participant. Test of significance between proportions in categorical variables were assessed using chi square test ($\chi 2$) in both groups. The means were compared using independent t-test while correlation between parameters were analyzed using Pearson correlation coefficient. **Results:** The mean age of the POAG participants was 57.16 + 13.3 years and the mean age of the non-glaucoma participants was 54.15 + 13.4 years. The mean IOP in the POAG group was 30.2 + 8.9mmHg while non- glaucoma group was 14.2 + 2.6mmHg ($P < 0.001$), other ocular parameters were not significantly different in both groups. In the POAG group, decreased spherical equivalent refractive error (i.e increasing myopia) was significantly associated with increased axial length ($r = -0.252$, $P = 0.01$), but not significant in the non- glaucoma group. However, in the non-glaucoma group, central cornea thickness increased with increasing intraocular pressure ($r = 0.305$, $P = 0.003$), which was not significant in the glaucoma group. **Conclusion:** Patients with POAG had much higher IOP and thus, IOP remains a significant risk factor in its development. There was a significant relationship between refractive state and axial length in the POAG group while a significant relationship was identified between central cornea thickness and intraocular pressure in the non- glaucoma group.

Keywords: *AL, CCT, glaucoma, IOP, non- glaucoma, ocular biometry, refractive state*

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Introduction

Glaucoma is a global health problem. It is the leading cause of irreversible blindness worldwide[1] as it is responsible for 8% of blindness among the 39 million people blind worldwide.[2] Africa has the highest prevalence of blindness due to glaucoma compared to other regions in the world accounting for about 15% of blindness with an increased prevalence of primary open angle glaucoma (POAG).[3] It has been reported that primary open angle glaucoma is about 4–5 times higher in blacks compared to Caucasians with an earlier age of onset and a fast progression of disease course.[4]

Glaucoma is a devastating and a huge health problem in Nigeria. It ranks as the second leading cause of blindness with a prevalence of 5.02% among adults 40years and older.[5] The number of individuals affected by glaucoma is much higher than the individuals known to have the disease, as glaucoma can remain asymptomatic in the early stages until it becomes severe resulting in blindness.[6] In Nigeria, about 50% of persons are already blind in one eye at presentation and with advanced damage in the other eye.[7,8] This could be attributed to the poor health seeking behaviour especially with the absence of pain which seems to be the driving force for presentation to the hospital.[9] Other factors such as the absence of visual loss in the early stages,[7] limited eye

How to cite this article: Oluwaniyi AT, Olawoye O, Sarimiye TF, K. Ajayi BG. Comparison of ocular biomery in primary open angle glaucoma and non-glaucoma in South West Nigeria. J West Afr Coll Surg 2023;13:37-44.

Received: 29-Oct-2022
Accepted: 05-Dec-2022
Published: 20-Mar-2023

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Access this article online

Website: www.jwacs-jcoac.com

DOI: 10.4103/jwas.jwas_264_22

Quick Response Code:

care facilities with unequal distribution (more in urban than rural areas), low literacy level, lack of awareness and poverty have also contributed to the late presentation and delayed diagnosis.[9] Thus, the need for early and accurate screening.

Case detection is often very difficult especially in developing countries such as Nigeria where there are resource constraints despite the increasing proportion of glaucoma cases. Early detection of glaucoma is important in reducing the rate of blindness from the disease. Hence, the need for a high index of suspicion in glaucoma diagnosis.

Ocular parameters such as intraocular pressure,[10,11] thin central cornea,[12-16] long axial length[17,18] and myopic refractive error[19,20] have all been documented as risk factors of glaucoma especially among Caucasians and African Americans, with little documentation in Africa where there's an alarming rate of blindness. Several studies have been done on the relationship between these ocular parameters in glaucoma and normal subjects with conflicting results.[21-26] An understanding of the influence of these ocular parameters and the relationship between these parameters in both glaucoma and non-glaucoma subjects can help explain the increased risk of an individual for glaucoma development. This information is important to understand their relevance (if any) in the development of glaucoma among continental Africans. The aim of this study is to assess ocular parameters such as intraocular pressure, central cornea thickness, axial length, refractive state and the relationships between them in POAG and non-POAG participants in South West Nigeria.

Ibadan is the capital of Oyo state, one of the six states that make up the South-west geo political zones in Nigeria. It is also the biggest city in Africa. Eleta Eye Institute is located in the heart of Ibadan, which is the most popular and densely populated area of Ibadan. It is a non-profit, hospital owned by the Catholic Arch Diocese of Ibadan. It lies adjacent to the St Mary's catholic hospital and it offers comprehensive eye care services which includes general ophthalmic, medical and surgical services. The patients come from Ibadan, surrounding towns and neighbouring states of Ogun, Osun, Ondo, and Ekiti and other parts of the country.

Materials and Methods

Study design

This was a comparative study.

Study population

Adult participants who were 30 years and older (consisting of 92 POAG and 92 non-glaucoma) of diverse ethnic and religious background attending the outpatient clinic of Eleta Eye Institute, Ibadan. The primary open angle glaucoma (POAG) group consists of newly diagnosed, previously untreated primary open angle glaucoma participants while the control group consists of participants without glaucoma, family history of glaucoma or any ocular pathology, presenting to the hospital for routine ophthalmological examinations.

Inclusion criteria

Participants aged ≥ 30 years old with visual acuity better than or equal to 6/60 in the absence of ocular pathologies, absence of systemic diseases and those without a previous history of ocular surgery were included.

Newly diagnosed cases of POAG in both eyes were defined as optic nerve head changes such as ≥97.5th percentile of the VCDR (≥0.7) or VCDR asymmetry (≥0.1) or a neuroretinal rim width reduced to less than or equal to 0.1 CDR, with a reliable standardized automated perimetry confirming visual field defects due to glaucoma;[27] open anterior chamber angles with at least visualization of scleral spur on gonioscopy without indentation (Shaffer's grading 3–4 in all quadrants); intraocular pressure > 21mmHg.

Non-glaucoma (controls) cases were defined as healthy participants with no ocular features suggestive of glaucoma i.e. VCDR <0.4, normal visual fields on standard automated perimetry, IOP <21mmHg, with no family history of glaucoma and not on treatment for glaucoma.

Also included was refractive error (calculated as the spherical equivalent which is the spherical refractive error plus half the cylindrical refractive error) on autorefraction ≥ -3D or < +3D. Myopes were defined as spherical equivalent -0.25D to -3D while hypermetropes were defined as spherical equivalent +0.25D to +3D.

Exclusion criteria

Participants less than 30 years old with visual acuity worse than 6/60, ocular and systemic diseases and those with previous history of ocular surgery were excluded from the study. Furthermore eyes with high degrees of ametropia (< -3D or > +3D) were also excluded.

Data collection process

Participants who met the inclusion criteria underwent detailed ophthalmological examinations including visual acuity measurement using Snellens and tumbling E chart, anterior and posterior segment examination, intraocular pressure (IOP) measurement using a calibrated Goldmann applanation tonometer, central cornea thickness (CCT) and axial length were measured using ultrasound pachymeter (Sonomed Pacscan Plus, Model 300AP+) and refractive error measurement (spherical equivalent) with Auto refractor (Zeiss Acuitus Model 5015).

Visual field analysis was also carried out using automated Humphrey visual field analyzer (2010 Zeiss Meditec HFA II 750). All measurements were taken before commencement of anti-glaucoma therapy in participants with glaucoma.

Data analysis

Data was analyzed using the statistical package for social sciences (SPSS) version 23.0. Proportions and percentages

were used for qualitative variables, while numeric data was presented in mean and range. Test of significance of qualitative variables between the two groups were assessed using chi square test ($\chi 2$). Test of significance of quantitative variables between the two independent groups was done using Independent t test. The relationships between parameters were analyzed using Pearson correlation (r). The correlation is referred to as weak if correlation coefficient (r) lies between 0.10 and <0.40, moderate if r is between 0.40 and <0.70, and strong if r is between 0.70–1.00. The p-value level of statistical significance was set at 0.05. Data was collected from both eyes but analysis was carried out in the right eye as there was a strong correlation between observations from both eyes across all variables.

Ethical considerations

The study was conducted in accordance to the tenets of Helsinki declaration. Ethical approval was obtained from the Ethical Review Board of the Sebastian Centre for Ophthalmic Research and Education, Eleta Eye Institute, Ibadan. A written informed consent was also obtained from each participant before being included in the study.

Result

A total of 184 participants were included in this study. The mean age of the participants with POAG was 57.16 ± 13.28 years and 54.15 ± 13.39 years in the non-glaucoma (control) group. There were more female participants in both groups, however no statistically significant difference was demonstrated between both groups for age and sex. [Table 1] displays the demographic and clinical characteristics of both groups.

[Table 2] compares the mean ocular parameters in the POAG and control groups. The mean IOP in the glaucoma

Table 1: Demographic and clinical characteristics of POAG and control groups

Variable	POAG (%) N=92	CONTROL (%) N= 92	p-value
Age (Mean±SD	57.16 ± 13.28	54.15 ± 13.39	0.127
30 – 39 years	10 (10.8)	13 (14.1)	
40 – 49 years	19 (20.6)	21 (22.8)	
50-59 years	17 (18.4)	26 (28.2)	
60-69 years	26 (28.2)	13 (14.1)	
70 years and above	20 (21.7)	19 (20.6)	
Sex			0.455
Male	41 (44.5)	36 (39.1)	
Female	51 (55.4)	56 (60.8)	
History of spectacle use			0.286
Yes	38 (41.3)	31 (33.7)	
No	54 (58.7)	61 (66.3)	
History of Hypertension			0.292
Yes	24 (26.0)	18 (19.5)	
No	68 (73.9)	74 (80.4)	
Family history of glaucoma	27 (29.4)	Nil	
Visual acuity in the better eye			<0.001*
≥ 6/18	66 (71.7)	85 (92.3)	
6/18 - 6/60	26 (28.2)	7 (7.6)	
VCDR	0.90 ± 0.11	0.27 ± 0.06	<0.001*
Average mean deviation (dB)	12.88 ± 5.97	-1.87 ± 0.67	

*Statistically significant at p<0.05, POAG- primary open angle glaucoma, VCDR- vertical cup to disc ratio

Table 2: Comparing ocular parameters in POAG and control groups

Variable	POAG N=92		CONTROL N=92		p-value
	Mean±SD	Range Min& Max	Mean±SD	Range Min& Max	
SE (Dioptre)					
Myopia	-1.25+0.9	-3 to -0.25	-1.04+1.0	-3 to -0.25	0.44
Hypermetropia	1.07+0.8	0.25 – 3	1.15+0.6	0.25 -3	0.55
IOP (mmHg)	30.2 ± 8.9	22.0–62.0	14.2 ± 2.6	10.0-20.0	<0.001*
CCT (µm)	513.5 ± 38.6	433.0-592.0	518.8 ± 31.6	421.0-616.0	0.21
AL (mm)	24.4 ± 0.8	21.4-25.7	24.2.±0.8	20.9-25.9	0.34

Statistically significant at 0.05 level, POAG- primary open angle glaucoma, SE- spherical equivalent, IOP- intraocular pressure, CCT- central cornea thickness, AL- axial length

group was 30.2 ± 8.9mmHg while the control group was 14.2 ± 2.6mmHg. This difference was found to be statistically significant ($P < 0.001$). There were more hypermetropes in both the POAG (68/92, 73.9%) and control (50/92, 54.3%) groups compared to myopes, although the number of myopes (33/92, 35.9%) in the POAG group were more than in the control group (19/92, 20.7%). The mean spherical equivalent in the POAG group was -1.25 + 0.9D for myopes and 1.07+0.80D for hyperopes while it was -1.04+1.0D and 1.15+0.66D for the control group respectively. There were no significant differences between the mean spherical equivalent ($P = 0.44$ and $P = 0.55$), central cornea thickness ($P = 0.21$) and axial length ($P = 0.34$) in the POAG and control groups.

The mean ocular parameters of different refractive states in POAG and control were compared in [Table 3]. A statistically significant difference (p=<0.001) was found between the mean IOP in the POAG and control groups for both myopes and hyperopes. No significant difference was demonstrated between the mean CCT ($P = 0.22$), ($P = 0.35$) and AL ($P = 0.29$), ($P = 0.83$) in both groups for myopes and hyperopes respectively.

[Table 4] shows the correlation between ocular parameters in the POAG group. Among all subjects in the POAG group, a statistically significant negative correlation (r= -0.252, $P = 0.01$) was found between refractive error and axial length such that axial length increases with increasing myopia. No significant correlation was found between other ocular parameters.

In POAG participants with myopia, no significant correlation was found between the ocular parameters but participants with hypermetropia showed a significant weak negative correlation (r= -0.389, $P = 0.02$) between refractive error and central cornea thickness. Thus, with increasing hypermetropia, central cornea thickness decreases.

As shown in [Table 5] below, there was a significant positive correlation between central cornea thickness and intraocular pressure in the control group. This correlation was also demonstrated by the control hypermetropes. Hence central cornea thickness increases with increasing intraocular pressure. However, central cornea thickness and axial length were positively correlated in the myopic subgroup such that longer eyes had thicker corneas.

Discussion

This study aimed at providing information on ocular parameters such as central cornea thickness, intraocular pressure, axial length and refractive state in subjects diagnosed with primary open angle glaucoma and controls.

The mean intraocular pressure in the POAG group was significantly greater than that of the controls ($P < 0.001$). This has been consistently reported by several studies, further emphasizing the importance of intraocular pressure as a significant, independent and modifiable risk factor of glaucoma.[28-30] In this study, the participants in the POAG subgroup had lower mean central cornea thickness than controls but the difference was not statistically significant

Table 3: Comparing ocular parameters in POAG and control groups of different refractive errors

Variable	Poag	Control	p- value
MYOPES			
IOP	30.73 + 8.6	13.47 +2.2	<0.001*
CCT	510.4+ 33.8	522.5 +34.3	0.22
AL	23.72 +0.8	23.46 +0.8	0.29
HYPERMETROPES			
IOP	29.22 +7.9	14.57+2.7	<0.001*
CCT	513.3+ 40.8	519.6 +33.13	0.35
AL	23.28 +0.7	23.25+0.8	0.83

* Statistically significant at 0.05 level, POAG- primary open angle glaucoma, IOP- intraocular pressure, CCT- central cornea thickness, AL- axial length

Table 4: Correlation analysis between ocular parameters of primary open angle glaucoma subjects

Variables	SE vs CCT	CCTvs IOP	SEvs IOP	SE vs AL	CCTvsAL
ALL SUBJECTS					
Pearson correlation (r)	0.036	0.174	-0.111	-0.252	0.134
P value	0.73	0.09	0.29	0.01*	0.20
MYOPIA					
Pearson correlation (r)	-0.010	0.098	-0.107	0.03	0.076
P value	0.95	0.58	0.55	0.84	0.67
HYPERMETROPIA					
Pearson correlation (r)	-0.389	0.081	0.108	-0.307	0.214
P value	0.02*	0.63	0.52	0.06	0.20

*statistically significant, SE- Spherical equivalent, CCT-Central corneal thickness, IOP- Intraocular pressure, AL- Axial length

Table 5: Correlation analysis between ocular parameters of control subjects

Variables	SEvs CCT	CCTvs IOP	SEvs IOP	SE vs AL	CCTvs AL
ALL SUBJECTS					
Pearson correlation (r)	-0.097	0.305	0.069	-0.157	0.187
P value	0.35	0.003*	0.50	0.13	0.07
MYOPIA					
Pearson correlation (r)	-0.375	0.095	-0.369	0.071	0.469
P value	0.11	0.69	0.12	0.77	0.04*
HYPERMETROPIA					
Pearson correlation (r)	0.085	0.484	-0.021	-0.172	0.033
P value	O.51	<0.001*	0.86	0.18	0.79

*statistically significant, SE- Spherical equivalent, CCT-Central corneal thickness, IOP- Intraocular pressure, AL- Axial length

(P = 0.21). Similar findings comparing central cornea thickness in POAG and control were reported by Mercieca *et al*.[31] in Nigeria and Ntim-Amposah *et al*.[32] in Ghana where central cornea thickness of POAG patients were found to be thinner than controls but was not statistically significant. However, the reports by La Rosa *et al*.[33] and Ventura *et al*.[34] in other studies showed that the central cornea thickness in glaucoma subjects were significantly thinner than controls.

Comparing the mean spherical equivalent in glaucoma and control groups showed no significant difference among myopes (P = 0.44) and hypermetropes (P = 0.55). This was also demonstrated by Yazdani *et al*.[35] where no significant difference was found between spherical equivalent in POAG and control (P = 0.354). In contrast, Elgin *et al*.[36] reported that patients with glaucoma were more myopic than controls (mean spherical equivalent -1.94 + 1.86 vs -0.76 +2.03 dioptres (P = 0.048). This difference could be attributed to the age group studied as the patients were much older in the present study and the study by Yazdani compared to the latter study. The participants in this study were more hypermetropic. It has been demonstrated that hypermetropia tends to increase with ageing.[37] This hypermetropic shift was attributed to a decrease in cornea and lens power with ageing.[37] Perhaps, the increase in the number of participants in the older age group in our study compared to the younger age group in the study by Elgin *et al.* could explain the slight hyperopic shift as opposed to myopia.

The mean axial length of the glaucoma group and control group were not significantly different (P = 0.34). This was also consistent with studies by Adewara *et al.*[30,32] and Tomais *et al*.[38] while Oku *et al*.[18] and Gupta *et al*.[39] in contrast, demonstrated that participants in the primary open angle glaucoma group had significantly longer axial length compared to the control group (P = 0.001). This difference could be attributed to a difference in the sample size as both studies had a larger sample size compared to the present study.

There's no general consensus as to how central cornea thickness varies with refractive error. In this study, all participants in the POAG and control group showed no association between the two parameters while in the POAG hypermetropic group, with increasing hypermetropia, the cornea had a tendency to become thinner (r= -0.389, P = 0.02). Similar to this study, Mavic *et al*.[40] in primary open angle glaucoma patients also found no correlation between the two parameters (r= -0.108, P = 0.615). Krishnan *et al*.[26] demonstrated that central cornea thickness increased with increasing myopia and vice versa in a normal population (r= -0.172, P = 0.03). This was also supported by Betiku *et al.*[41] In contrast Chang *et al*.,[21] showed that central cornea thickness was positively correlated with refractive error as central cornea was found to be thinner in more myopic eyes, however this was not statistically significant. They suggested that a decrease in cornea thickness is as a result of anterior segment changes as the eyeball elongates in myopes. The study population were however younger compared to the present study.

Furthermore, the correlation between central cornea thickness and axial length was not significant (r= 0.134, P = 0.20) in the POAG group but significant in the control myopic group (r= 0.469, P = 0.04) such that as the axial length increased, the central cornea thickness also increased. This finding was consistent with studies of Betiku *et al.* in Nigeria,[41] Lee *et al*.[42] in Korea and Krishnan *et al*.[26] in India (in a healthy population) which showed that an increase in axial length was associated with a corresponding increase in central cornea thickness. Lee *et al*.[42] suggested the possibility of the development of a passive protective mechanism against cornea thinning as the eye ball elongates which could vary based on genetic, ethnic or environmental factors.

Shimmoyo *et al*.,[43] Olivera *et al*.[44] and Tomais *et al*.[38] on the other hand found no correlation between the two parameters in subjects with glaucoma as reported in this study while Solu *et al*.[45] and Chang *et al*.[21] in a group of healthy subjects reported that there was a significant decrease in central cornea thickness as axial length increases. The finding of the present study therefore is at variance with the theory of cornea thinning as a marker for sclera thinning and a thin scleral bed of lamina cribosa associated with elongated eyes which is said to be a predisposing factor in

the development of glaucoma.[43,46] Olivera *et al*.[44] noted that the effect of thin CCT on glaucoma risk other than IOP estimation might just be theoretical but however suggested that direct *in vivo* measurement of scleral thickness might provide more insight into the relationship between thin CCT and scleral thickness.

There was a significant inverse correlation between refractive state and axial length in the POAG group (r= -0.252, P = 0.01) but not significant in the control group (r= -0.157p=0.13) such that as axial length increased, there was an increase in myopic refractive state. This was consistent with that reported by some studies.[39,47] Gupta *et al*.[39] showed that as axial length increased, the severity of myopia increased in both glaucoma group and controls but added that the glaucoma group had a significantly longer axial length (P < 0.001) compared to controls which could have predisposed to the increased risk of development of glaucoma. Cahane *et al*.[48] demonstrated in a model that eyes with long axial length and thin sclera are predisposed to increased tension within the lamina cribosa which increases the risk of damage to nerve fibers coursing through it.

There have been several reports of a correlation between intraocular pressure and refractive error. The relationship between refractive error and intraocular pressure in this study was not significant in both groups which is similar to the findings of Chinawa *et al*.[49] who noted a poor correlation between intraocular pressure and myopia. They suggested the possibility of mechanisms other than intraocular pressure playing a role in the development and progression of myopia. Mathapathi *et al*.[50] also found no correlation between intraocular pressure and low, moderate myopia and hypermetropia consistent with this study but reported that there was a significant correlation between intraocular pressure and high myopia. Glaucoma genes were suggested to play a vital role in the development of high ocular tension among high myopes. Nomoura *et al*.,[51] demonstrated that intraocular pressure significantly increased with advancing degrees of myopia, even after controlling for factors such as central cornea thickness and age (P = 0.011). This observation was also supported by Osaiyuwu *et al.*[52] Theories surrounding the interaction between increasing degrees of myopia and intraocular pressure have been inconclusive. It was suggested that increasing levels of intraocular pressure results in gradual stretching of the eyeball leading to myopia[53] while others suggested that increase in scleral tension within the lamina cribosa results in increased susceptibility to damage in myopes even when the intraocular pressure is normal.[54]

A positive relationship was found between CCT and IOP in the present study. There was a significant increase in IOP with an increase in CCT in the control group (r=0.305, P = 0.003) but not significant in the glaucoma group (r= 0.174, P = 0.09). This is consistent with the report of several hospital and population-based studies.[55-58] Herndon *et al*.[57] and Soriano *et al*.[58] found no significant relationship between CCT and IOP in glaucoma patients but noted a significant relationship in controls and ocular hypertensives respectively. It was suggested that CCT may be an independent factor unrelated to other ocular parameters in the pathogenesis of glaucoma. Iyamu *et al*.,[59] found a significant relationship between CCT and IOP among ocular hypertensives but noted that the relationship was not significant in glaucoma patients and controls. In contrast, Tonnu *et al*.[60] and Gelaw *et al*.[61] reported that there was a significant positive association between CCT and IOP in glaucoma patients. Hence, the impact of a thin cornea in the underestimation of intraocular pressure with resultant delay in treatment should always be considered by a clinician. Variations in instruments used in the measurement of ocular parameters, study designs, age and size of the study population could play a pivotal role in disparities in study results. The limitations of the study includes, the hospital based setting which could have introduced selection bias and the small sample size of the study population.

Conclusion

There was a significant increase in intraocular pressure in the POAG group compared to control group which further emphasizes the importance of intraocular pressure as an independent, modifiable risk factor of primary open angle glaucoma. There is no difference in other ocular parameters between the two groups. Myopia increased with increasing axial length in the POAG group. IOP increased with an increase in CCT in the control group. Thus, the importance of pachymetry in the interpretation of intraocular pressure measurement. This study as compared to others suggests that variations exist in the relationship between ocular parameters. This is the first study, to the best of the authors' knowledge that will compare the relationship between these ocular parameters in glaucoma and controls in Nigeria.[28,30,41,47,51,52,55,56,59] More studies with larger sample size representative of the general population are needed to elucidate on the exact role (if any) of the relationship between these ocular parameters in the pathogenesis of glaucoma.

Acknowledgement

The authors gratefully acknowledge research assistant Ms Ibukun, ophthalmic nurse Ms Ronke Osho, refractionist Mr Taiwo and ophthalmic technician Mr Adebayo Gabriel for their invaluable contribution to this project.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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