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Prevalence and risk factors of obesity among undergraduate student population in Ghana: An evaluation study of body composition indices

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ORIGINAL RESEARCH

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Prevalence and risk factors of Vernal Keratoconjunctivitis among a Ghanaian clinical cohort: A case-control study

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Abstract

Background: Vernal Keratoconjunctivitis (VKC) has been determined to be highly prevalent in countries within the tropical climate region. However, little evidence from studies conducted within this region has been put forward to support this claim.

Aim: To determine the prevalence and risk factors of VKC among a Ghanaian clinical cohort.

Methods: A 3-year case-control study was conducted in a tertiary eye care institution, and medical records of patients who had been diagnosed of VKC between 2018 and 2021 were reviewed.

Results: Medical records of 3800 patients were reviewed. Some 359 cases of VKC were identified, with a population prevalence rate of 9.45%. Males comprised 57.1% of the population with VKC, with a male-to-female ratio of 1.33 : 1. The disease was more prevalent (40.8%) in children (≤17 years), and the overall odds of incidence decreased by 10% for a unit increase in age. Age and sex-adjusted models revealed significant positive associations between Keratoconus [aOR = 40.760, 95% CI −5.948 to 339.937], Rhinitis [cOR = 5.183, 95% CI −2.074 to 12.022] and VKC. However, the incidence of VKC was relatively less expressive among pterygium cases [cOR = 0.315, 95% CI −0.077 to 0.846].

Conclusion: VKC is highly prevalent among children and is often associated with comorbidities of atopic origin that exacerbate the impact of the disease among this vulnerable population. It is imperative that clinicians provide holistic care for children with VKC.

KEYWORDS

pterygium, rhinitis, risk factor, sickle cell, Vernal Keratoconjunctivitis

1 | INTRODUCTION

Vernal Keratoconjunctivitis (VKC) is a severe, sight-threatening ocular allergic disorder that affects both the tarsal and bulbar conjunctiva.[1] Although the allergic nature of the disease has long been accepted, its exact etiology and pathogenesis remain unclear.[2] The disease is typically seen in children and can severely affect the quality of life.[3]

The global distribution of VKC highlights varying incidences across different parts of the world.[4] While it remains an uncommon ocular allergic disease condition in other climate regions, VKC has been observed to be one of the leading reasons for hospital visits in countries within tropical regions, accounting for 3%–6% of patients of all ages.[5–8] This proportion is significantly higher among children and adolescents, where it has been estimated to be between 33% and 90%.[6,8,9] A population prevalence of 4–5% has been observed among African children.[6,8,9] In comparative case series across Europe and Asia, a higher proportion of boys were affected than girls; however, this gender-based disparity was not consistent with some studies conducted within Africa, with the distinction becoming less pronounced with increasing age.[5,8–11] These differences have been attributed to diversities in genetic makeup, environment (climate, socioeconomic status, and living styles), and gene-environment interactions.[12]

Generally, the disease usually begins before the age of 10 years, with the earliest age of onset being 5 months.[12,13] It usually resolves within 4–10 years after onset.[13,14] The disease occurs more commonly in males, with the distribution of males to females reported to vary from 4:1 to 2:1.[11,15,16] In atypical cases of adult onset, the distribution between males and females becomes almost equal.[11,13]

Based on the presence of limbal conjunctival gelatinous hypertrophy or upper tarsal conjunctival papillae, VKC can be accurately classified as palpebral, bulbar, or mixed.[17,18] VKC typically manifests bilaterally and has a poor visual prognosis if not managed adequately.[19] Common ocular complications include steroid-induced cataracts and glaucoma from treatment with corticosteroids, corneal scarring, microbial keratitis, and limbal tissue hyperplasia.[20]

VKC is known to be commonly associated with pre-existent atopic diseases such as asthma.[11] Atopy is more commonly associated with tarsal VKC than the limbal type.[21] Morbidities commonly associated with VKC include amblyopia, which is caused by corneal opacities, irregular astigmatism and keratoconus, and dry eye syndrome resulting from unsupervised use of corticosteroids.[22]

Endocrine, genetic, neurogenic, environmental, and socio-economic risk factors have been identified as being associated with the incidence of VKC.[11,21,23–25] Endocrine risk factors have been suggested by the sexual disparity in VKC prevalence,[23] and the overexpression of estrogen and progesterone receptors by conjunctival eosinophils within the conjunctival epithelium in people with VKC.[26] Additionally, growth factors neuropeptides and prostaglandins have been detected in high quantities in VKC.[27–29] Differences in prevalence of VKC observed among different racial groups and the identification of disease susceptibility genes for VKC through linkage analysis, support the role of genetic risk factors.[2] The incidence of the disease has also been linked to exposure to particulate matter from smoke and ultraviolet light.[27] In a nested population-based case-control study that evaluated the association between VKC and socioeconomic status among school children in Rwanda, high socioeconomic status was identified as an independent risk factor for VKC.[23]

VKC has been determined to be highly prevalent in countries within the tropical climate region.[11,25,30,31] However, little evidence from studies conducted within this region has been put forward to support this claim. This study hence sought to determine the prevalence and risk factors of VKC among a Ghanaian clinical cohort.

2 | METHOD

This 3-year case-control study[23] was conducted in a tertiary eye care institution (Dr. Agarwal's Eye Hospital) in Accra, Ghana. Data on individuals of all age groups who had been diagnosed with VKC between 2018 and 2021 were collected. The diagnosis was made on the grounds of the patient's medical history, characteristic symptoms reported, and clinical findings.

2.1 | Data collection procedure

Records of patients' ages, sex, ocular and medical histories, and age at onset of disease were extracted. Best-corrected visual acuities of the patients, as well as clinical findings documented after thorough examinations with a slit lamp biomicroscope were recorded. Similar data for a control group comprising healthy individuals were extracted. It was ensured that these individuals had no inherent ocular pathological conditions and were emmetropes (spherical equivalent of ±0.25 DS) with best corrected visual acuities of 6/6 in both eyes (Snellen).

2.2 | Diagnostic criteria

Complete ocular examination with a slit lamp biomicroscope, as well as the clinical diagnosis of VKC were carried out by an experienced ophthalmologist. The diagnosis was made on the grounds of patient medical histories (of atopic conditions such as asthma, rhinitis, and eczema), symptoms reported and pertinent clinical findings, and the criteria considered included;

1. The presence of conjunctival tarsal (cobblestone) and/or limbal papillae (Horner-Trantas dots), as hallmark signs of the disease, and
2. Recurrent symptoms of the disease (such as ocular itching followed by photophobia, mucoid discharge, watering, redness, and foreign body sensation).

TABLE 1 Background characteristics of the study population.

Characteristics	N (%)	VKC	Non-VKC	χ^2	p Value
Age				223.64	<0.001
0–17	1,552 (40.8%)	273 (7.2%)	1,273 (33.5%)		
18–35	1,928 (50.7%)	79 (2.1%)	1,849 (48.7%)		
36–59	278 (7.3%)	2 (0.1%)	276 (7.3%)		
60+	42 (1.1%)	(0.0%)	42 (1.1%)		
Sex				**21.72**	**<0.001**
Female	2073 (54.6%)	154 (4.1%)	1919 (50.5%)		
Male	1727 (45.4%)	205 (5.4%)	1522 (40.1%)		
Residence				4.12	0.13
Urban	3494 (91.9%)	340 (8.9%)	3154 (83.0%)		
Peri-urban	306 (8.03%)	19 (0.5%)	287 (7.53%)		
Ethnicity				0.91	0.92
Akan	1952 (51.4%)	182 (4.8%)	1770 (46.6%)		
Mole-dagbon	810 (21.3%)	78 (2.1%)	732 (19.3%)		
Ga-adangbe	542 (14.3%)	56(1.5%)	486 (12.8%)		
Ewe	438 (11.5%)	38 (1.0%)	400 (10.5%)		
Guan	58 (1.5%)	5 (0.1%)	53 (1.4%)		

Abbreviation: χ^2, Chi-square.

2.3 | Statistical analysis

Statistical analysis was carried out with IBM SPSS version 26 (SPSS Inc.). The chi-square (χ^2) test and univariable, and multivariable logistic regressions were used to determine the association between VKC and independent variables. Crude odds ratios were reported to show the strength of the association between the outcome and the two categorical independent variables (ocular disease with 8 levels and systemic diseases with 4 levels). To adjust for possible confounding effects, a multivariable logistic regression model was formulated to evaluate VKC risk factors. Both independent variables, ocular diseases and systemic diseases, were entered for the multivariable regression model without any exclusion based on significance. Adjusted odds ratio, 95% confidence interval (CI), and two-sided *p* Value were calculated. A *p* Value less than 0.05 was considered statistically significant.

2.4 | Ethical consideration

The study protocol was approved by the institutional review board of the University of Cape Coast (UCCIRB/CHAS/2022/81). Permission was sought from the management of Dr. Agarwal's Eye Hospital, and patient anonymity and confidentiality were ensured. Informed consent was waived since medical records were used. Investigators had access to patient-identifiable information, but these were not reported anywhere in the study. The study abided by the tenets of the Declaration of Helsinki.

3 | RESULTS

3.1 | Baseline characteristics of the study participants

Out of the 3800 medical records that were reviewed, the majority (91%) were for individuals who were younger than 36 years of age. Frequencies, and percentages of study participants across key demographic features, as well as the distribution of reported cases of VKC and their associations with demographics, are presented in Table 1. More than half of the study population were females (54.6%). There were 359 reported cases of VKC, indicating an overall study population prevalence rate of 9.45%. Of the 359 reported cases, 273 (76%) and 79 (22%) cases were identified among participants aged between 0–17 and 18–35 respectively. No cases of VKC were identified among the aged (60+ cohort). There were more reported cases of VKC among males (n = 205, 57.1%) compared to females (n = 154, 42.9%). A chi-square test revealed significant associations between the prevalence of VKC and age and sex respectively (Table 1). No associations were found between the incidence of VKC and ethnicity and place of residency, respectively.

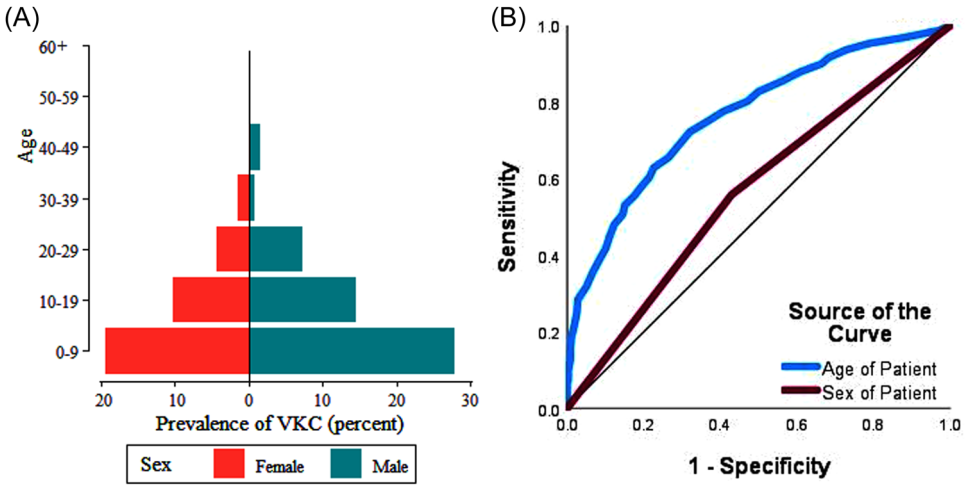

FIGURE 1 (A) Distribution of the prevalence of VKC across age and sex. (B) Age- and sex-specific receiver operating characteristic (ROC) curve analysis of the incidence of VKC. VKC, Vernal Keratoconjunctivitis.

TABLE 2 Distributions of ocular and systemic diseases and associated prevalence of VKC.

		Systemic diseases					
		Asthma (n = 137)	SCD (n = 28)	Rhinitis (n = 23)	None (n = 3612)	Cases of VKC	Condition-specific prevalence
Ocular disease	Glaucoma (n = 58)	4	0	0	54	1	1.72%
	Cataract (n = 35)	0	1	0	34	2	5.71%
	Dry eyes (n = 50)	0	0	1	49	0	0%
	Keratoconus (n = 5)	0	0	0	5	3	60%
	Others (n = 147)	3	1	0	143	9	6.12%
	Pinguecula (n = 32)	0	0	0	32	0	0%
	Pterygium (n = 88)	1	0	0	87	3	3.41%
	No disease (n = 3385)	129	26	22	3208	341	10.07%
Cases of VKC		12	2	8	337	359	9.45%
Condition-specific prevalence		8.76%	7.14%	34.78%	9.33%	9.45%	

3.2 | Age-sex prevalence analysis of VKC

The incidence of VKC was found to be age and sex-related (Table 1), and we further explored their degree of associations and evaluated the predictiveness of age and sex for modeling the incidence of VKC (Figure 1A).

The age distribution of the incidence of VKC was similar across gender. In a ROC analysis, both age and sex had significant areas under the curve (Figure 1). Age was identified as having the most predictive information on the incidence of VKC with an area under the curve (AUC) of 0.76 (95% CI: 0.74–0.79) (Figure 1A). We found that the overall odds of incidence of VKC decreased by 10% for a unit increase in age. The progression was such that the incidence of VKC among children aged between 0 and 17 was 80%, 96%, and 150% more likely compared to individuals aged between 18–35, 36–59, and 60+ respectively. The AUC for sex was 0.56 (95% CI: 0.53–0.60) (Figure 1B). The incidence of VKC was found to be 1.5 times more likely in males compared to females (Table 2).

3.3 | Associations of ocular and systemic diseases and incidence of VKC

Table 2 presents the distributions of the incidence of VKC across participants with ocular and systemic diseases.

Overall, pterygium was the most commonly reported ocular condition (2.3%), followed by glaucoma (1.5%) and dry eyes (1.3%) whereas keratoconus was the least reported condition (0.13%). Out of the five reported keratoconus, 3 (60%) of them had VKC. The prevalence of VKC among the study population with no ocular

disease was 10.07% (341/3385). All the systemic disease population cohorts had condition-specific prevalence above 6%. Of particular interest was Rhinitis, which had a higher condition-specific prevalence of 34.78% (8/23) compared to the 9.33% prevalence among the general population with no reported systemic diseases.

To establish the significance or otherwise of the relationships between ocular and systemic diseases and the incidence of VKC, both univariable and multivariable logistic regression analyses were carried out (Table 3). All the reported model parameter estimates were age-gender. Among participants with ocular diseases, the univariable analysis revealed that individuals with reported keratoconus and pterygium had significant rates of VKC compared to the population who reported no ocular conditions. For instance, compared to the healthy population, individuals with keratoconus were over 13 times [cOR = 13.39, 95% CI – 2.21 to 101.91; $p = 0.01$] more likely to develop VKC. Contrary, pterygium was identified as a tentative protective factor (i.e., adverse risk factor) for VKC, because compared to the healthy population, individuals with this ocular condition were approximately 68% [cOR = 0.32, 95% CI – 0.08 to 0.85; $p = 0.04$] less likely to develop VKC. In the multivariable analysis, the adjusted odds ratios (with 95% CIs) are reported (Table 3).

Keratoconus was the only ocular risk factor for VKC, such that, having adjusted for all other ocular and systemic conditions, individuals with keratoconus were 40 times more likely to develop VKC [aOR = 40.76, 95 % CI – 5.95 to 339.94; $p < 0.001$]. It is important to highlight that the upper bounds of the 95% CIs for the adjusted odds for glaucoma (2.19), cataract (2.97), and pterygium (2.43) indicate that it is possible to have a higher prevalence (about two times more likelihood) of VKC in some populations with these conditions compared to a healthy population.

Concerning participants with reported systemic diseases, Rhinitis was identified as a significant risk factor for VKC (Table 3). The univariable analysis revealed that compared to the population cohort with no reported systemic diseases, individuals with Rhinitis were five times more likely to develop VKC [cOR = 5.18, 95% CI –2.07 to 12.02; $p < 0.001$]. The reported adjusted odds ratio [aOR = 2.41, 95% CI – 0.92 to 5.93; $p = 0.06$] indicates that the incidence of VKC was two times higher among patients with Rhinitis, having adjusted for all other ocular and systemic conditions. Asthma and sickle cell disease were not identified as significant risk factors for VKC in both univariable and multivariable analyses (Table 3).

4 | DISCUSSION

The mainstay settings for prevalence studies of VKC has been the school and the clinic/hospital. A hospital-based setting was where this current study was conducted. It has the benefit of capturing the expected cases to elucidate their associated characteristics besides accuracy of diagnosis by expert clinicians. The study has the strength of a case control study suitable for a relatively rare disease like VKC. The scarcity of research from Sub-Saharan Africa (SSA) on VKC has been noted, and for this reason, VKC-related studies have been

TABLE 3 Age-gender adjusted logistic regression analysis of ocular and systematic disease associations with Vernal Keratoconjunctivitis.

	Univariable analysis			Multivariable analysis		
Variables	**Est. (SE)**	**cOR (95% CI)**	***p* Value**	**Est. (SE)**	**aOR (95% CI)**	***p* Value**
Ocular diseases						
Glaucoma	−1.85 (1.01)	0.16 [0.01–0.71]	0.07	−0.77 (1.02)	0.47 [0.03–2.19]	0.45
Cataract	−0.61 (0.73)	0.54 [0.09–1.79]	0.40	−0.16 (0.75)	0.85 [0.13–2.97]	0.83
Dry eyes	−20.38 (11.24)	<0.001 [<0.001–0.00]	0.99	−19.32 (10.36)	<0.001 [<0.001–0.00]	0.99
Keratoconus	2.60 (0.92)	13.39 [2.21–101.91]	**0.01**	3.71 (0.98)	40.76 [5.95–339.94]	**<0.001**
Pinguecula	−20.38 (14.05)	<0.001 [<0.001–0.00]	0.99	−19.25 (13.58)	<0.001 [<0.001–0.00]	0.99
Pterygium	−1.16 (0.59)	0.32 [0.08–0.85]	**0.04**	−0.14 (0.61)	0.87 [0.21–2.43]	0.82
Others	−0.54 (0.35)	0.58 [0.27–1.09]	0.12	−0.32 (0.36)	0.73 [0.34–1.40]	0.38
None	0	1	-	0	1	-
Systemic diseases						
Asthma	−0.07 (0.31)	0.93 [0.49–1.64]	0.82	−0.05 (0.32)	0.95 [0.49–1.71]	0.88
Sickle cell	−0.29 (0.74)	0.75 [0.12–2.52]	0.69	−0.35 (0.76)	0.71 [0.11–2.56]	0.65
Rhinitis	1.65 (0.44)	5.18 [2.07–12.02]	**<0.001**	0.88 (0.47)	2.41 [0.92–5.93]	0.06
None	0	1	-	0	1	-

Note: Comparison by univariable and multivariable logistic regression; *p* values less than 0.05 were deemed significant. Bold value represents significant *p* values.

Abbreviations: aOR, adjusted odds ratio; cOR, crude odds ratio; Est, parameter estimate; SE, standard error.

advocated, given the particularities of the disease in the sub-region.[32] This is more so as most existing studies on ocular allergy are not exclusive to VKC.[33-35] This case-control study is the first which focused exclusively on assessing the prevalence and risk factors associated with VKC in a large clinical cohort in Ghana. The prevalence of VKC among the study sample is within the middle bracket reported for most SSA countries that is, 2.30%–37%[32] but within the upper limit of reported cases in Europe (ranges from 1.2 to 10.6 cases per 10,000 population).[36] The high prevalence in SSA has been linked to the hot climatic conditions in such countries as Ghana, poor socioeconomic status, air pollution, and other comorbidities.[37] The variation in the prevalence has been attributed to the diverse geographic and climatic spread.[32] This gives credence to the necessity for jurisdictional-specific prevalence studies of VKC and further supported the region-to-region variation within the same country. The prevalence of 9.45%, though at the point of care could be far less than what exists in the population because barely half of the children (the most affected age group) receive care, and for those who do only 17% visit the clinic two times in a year.[8]

A general male predominance in the disease was observed for all age groups, with males being 1.54 times more likely to develop VKC than females, with a male-to-female ratio of 1.33:1. Higher susceptibility to VKC among males has been observed in multiple studies in countries within tropical regions across the world, highlighting a possible general genetic predisposition.[4,38–40] This pattern of distribution has been attributed to the purported role of estrogen and progesterone in the pathogenesis of the disease, as these hormones have been hypothesized to influence the action of eosinophils in patients with VKC through their receptors.[41] The converse has however been found in studies involving Nigerian populations where equal male-to-female distributions[42,43] or female predominance[30,44] in all types of VKC have also been reported.

Children were found to have the greatest susceptibility to VKC in this study. VKC is known to be a childhood disease, with ages of onset usually between 4 and 9 years.[2,30] Studies that assessed the demographic and clinical profile of VKC reported a mean age of presentation of the disease as 12 years, with about 12% of patients above 20 years of age.[45,46] Kawuma et al.[46] proposed that environmental factors such as uncontrolled exposure to ultraviolet light, and allergens in dust and pollen are responsible for this trend.[46] It is argued that children are particularly at risk since they spend much of their time outdoors. The disease has been reported to strongly and negatively affect the quality of life of afflicted children since limitations are imposed on their daily activities in an attempt to prevent the worsening of the disease.[29] Discomforts caused by the disease, coupled with multiple review appointments geared at monitoring the regression of the disease lead to time lost from school and academic work. This has, in several cases, led to poor academic performance.[47] The prevalence sharply declines from early adulthood (Figure 1A) and is virtually nonexistent.

Keratoconus was found to be statistically associated with VKC in this study. Keratoconus is a known complication of chronic VKC, and its prevalence varies according to geographical area.[48] Its prevalence has been reported to be high in India, a country within the tropical climate region,[45] and low in countries within temperate climate regions.[49] Totan et al.[50] in their case series demonstrated that patients with VKC had abnormal corneal topography pattern on videokeratography. Corneal topographic patterns seen in VKC and similar to Keratoconus include asymmetric bow tie with inferior steepening, superior steepening, high corneal irregularity, and high corneal asymmetry index.[51] The association between VKC and Keratoconus has been postulated to be caused by frequent eye rubbing, which leads to the release of inflammatory mediators such as matrix-metalloproteinase-13, IL-6, and tumor necrosis factor-alpha in response to microtrauma.[52–54] Considering this significant association, all patients with VKC must be screened for the presence of Keratoconus.[55] In light of the progressive course of pediatric Keratoconus,[56] and the high prevalence of VKC among children, such screening would allow for early detection and the initiation of disease-modifying treatments such as corneal crosslinking, to halt the progression of Keratoconus.[57] Pterygium was identified as a potential protective factor for VKC. There is a lack of understanding of the relationship between pterygium and VKC. There is therefore a need for further research to gain a more in-depth understanding in this area.

Patients with Rhinitis were found to be more than fivefolds likely to develop VKC than patients with other systemic disease conditions. This is consistent with studies that sought to determine the association between systemic atopic conditions and VKC, where patients were found to have a medical history of allergic Rhinitis.[11,14] In another study that sought to determine the pattern and mode of presentation of VKC among a Nigerian cohort, a history of atopic diseases such as Asthma and Rhinitis was present in 4.50% of the population.[30] The association between VKC and Rhinitis, as diagnosed by an otolaryngologist is not well-established yet.[58] Nevertheless, the association is believed to be hinged on their common immunopathology—fixation of IgE molecules on the surface of mast cells and release of mediators such as histamine and prostaglandins which mediate type I immune reactions.[7,58,59] Given this similarity, it is advocated that VKC should be considered in future guidelines on the prevention of the development of Allergic Rhinitis especially in childhood.

A possible limitation of the study is that it only includes information on a subset of patients with VKC, likely those with the most severe cases of the disease. The hospital-based design of the study may have inadvertently excluded VKC patients with less severe forms of the disease and poor health-seeking behavior, which could have influenced the reported estimates.

5 | CONCLUSION

VKC is highly prevalent among children and is often associated with comorbidities of atopic origin that exacerbate the impact of the disease among this vulnerable population. It is imperative that clinicians provide holistic care for children with VKC.

AUTHOR CONTRIBUTIONS

Samuel Kyei: Conceptualization; investigation; funding acquisition; writing—original draft; methodology; validation; visualization; writing—review and editing; project administration; supervision; resources. **Mary Nkansah**: Investigation; funding acquisition; writing—original draft; software; writing—review and editing; visualization; validation; data curation; resources. **Kofi Asiedu**: Conceptualization; investigation; funding acquisition; writing—original draft; validation; visualization; writing—review and editing; supervision; project administration; resources. randy asiamah: investigation; funding acquisition; writing—original draft; validation; visualization; writing—review and editing; formal analysis; resources. **Ebenezer Zaabaar**: Investigation; funding acquisition; writing—original draft; validation; visualization; writing—review and editing; resources. **Ebenezer Afrifa-Yamoah**: Investigation; funding acquisition; writing—original draft; writing—review and editing; visualization; validation; formal analysis; resources; project administration.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

ETHICS STATEMENT

The study protocol was reviewed and approved by the institutional review board of the University of Cape Coast (UCCIRB/CHAS/2022/81). Permission was sought from the management of Dr. Agarwal's Eye Hospital, and patient anonymity and confidentiality were ensured.

TRANSPARENCY STATEMENT

The lead author Samuel Kyei affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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